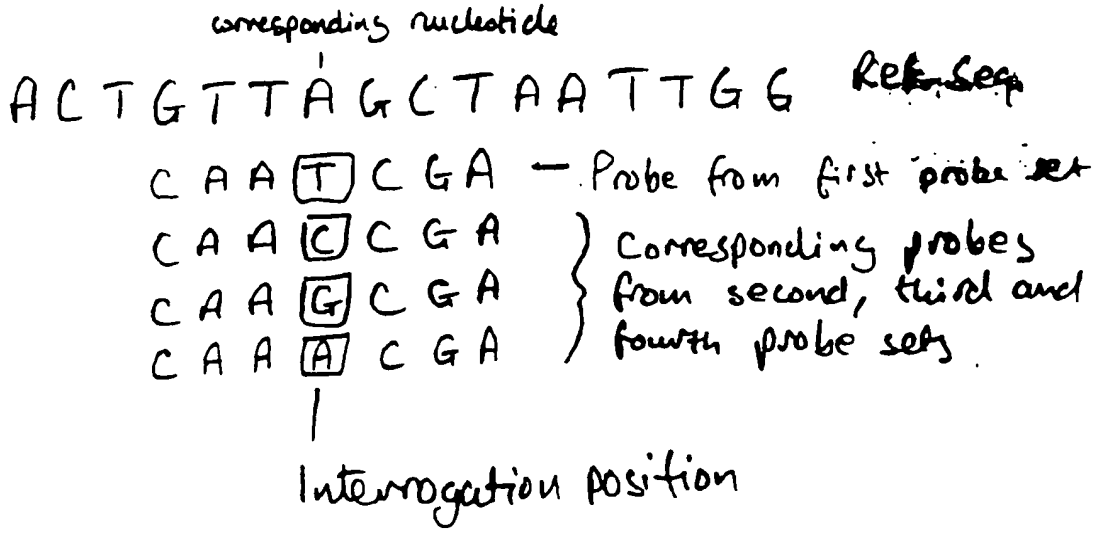
corresponding nucleotide
ACTGTTAGCTAATTGG Ref. Seq
CAATCGA — Probe from first probe set
CAACCGA
CAAGCGA
CAAACGA
} Corresponding probes from second, third and fourth probe sets
Interrogation position

Fig. 1

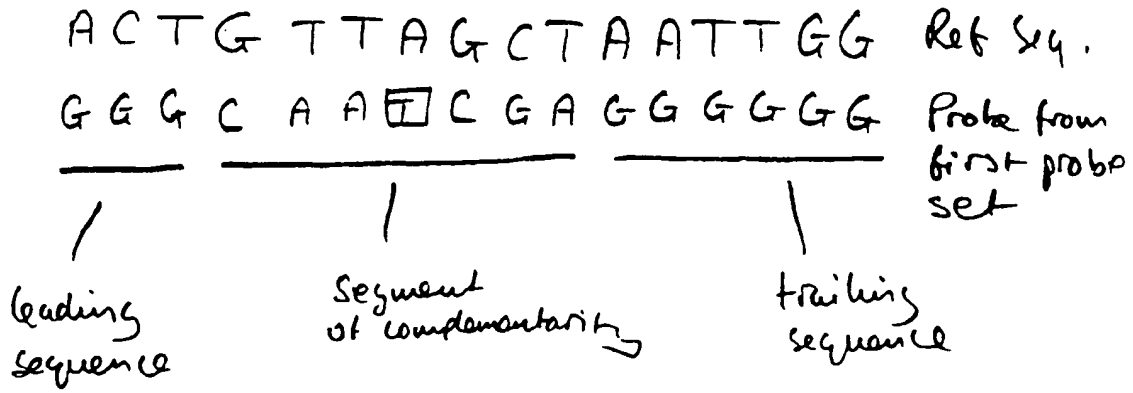
ACTGTTAGCTAATTGG Ref Sq.
GGGCAATCGAGGGGGG Probe from first probe set
leading sequence
Segment of complementarity
trailing sequence

Fig. 2

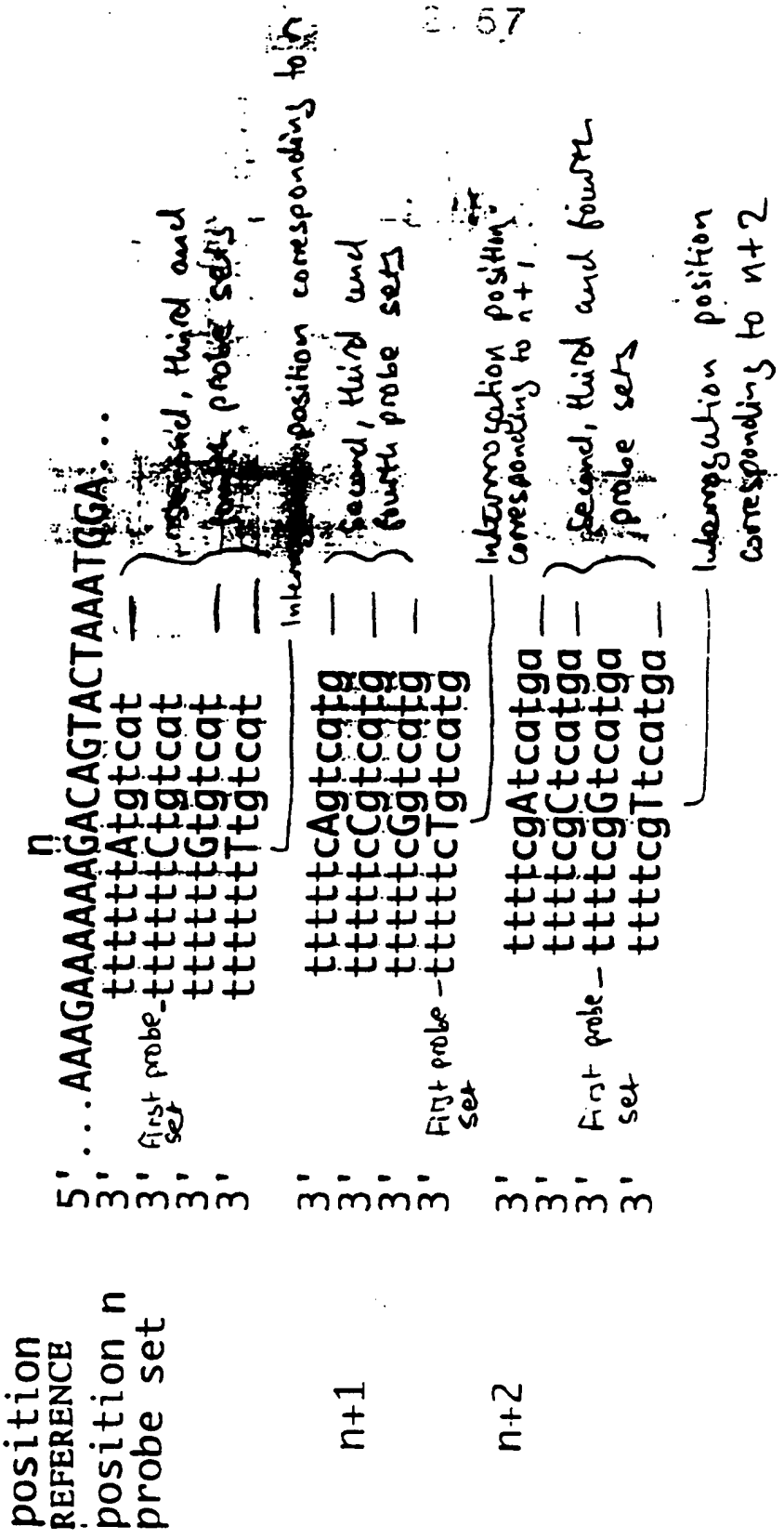
position
REFERENCE
position n
probe set
n
5' ...AAAGAAAAAAGACAGTACTAAATGGA...
3' ttttttAtgtcat
3' First probe-ttttttCtgtcat
set
3' ttttttGtgtcat
3' ttttttTtgtcat
3' tttttcAgtcatg
3' tttttcCgtcatg
3' tttttcGgtcatg
3' First probe -ttttttcTgtcatg
set
n+1
3' ttttcgAtcatga
3' ttttcgCtcatga
3' First probe- ttttcgGtcatga
set
3' ttttcgTtcatga
n+2

Fig. 3

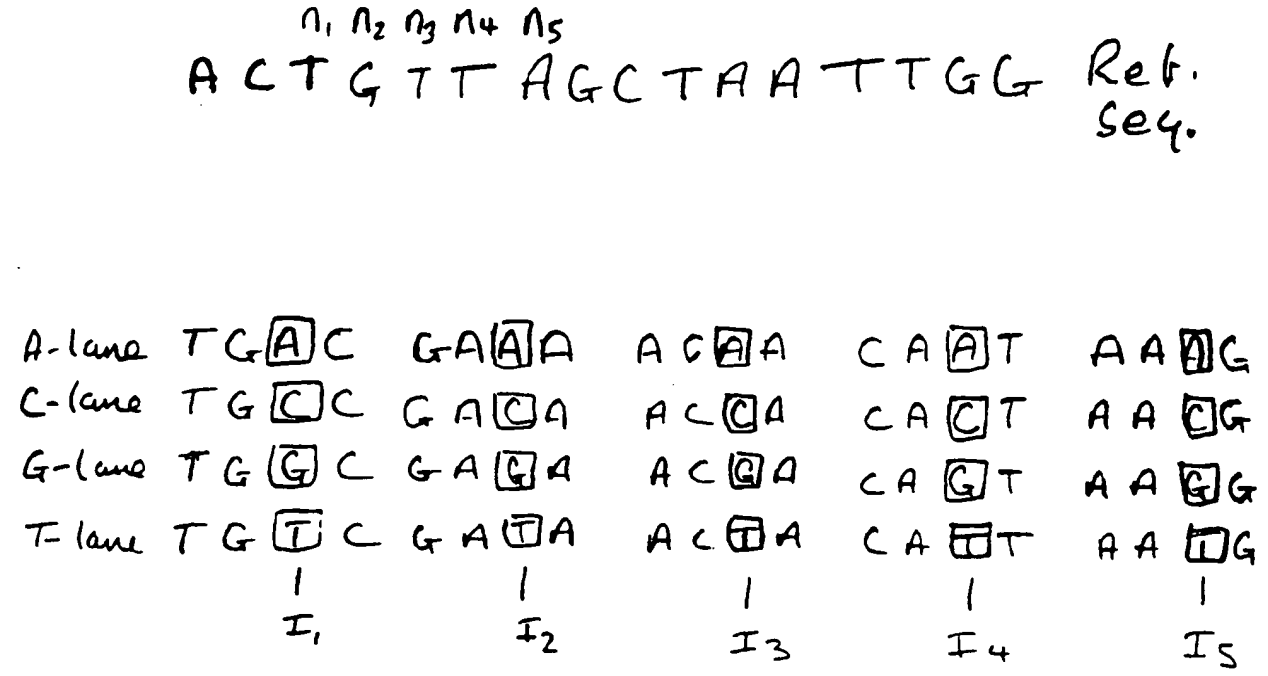
n1 n2 n3 n4 n5
A C T G T T A G C T A A T T G G Ref. seq.
A-lane T G A C G A A A A C A A C A A T A A A G
C-lane T G C C G A C A A C C A C A T A A C G
G-lane T G G C G A G A A C G A G T A A G G
T-lane T G T C G A T A A C T A T T A A T G
I1 I2 I3 I4 I5
wt. lane T G A C G A C A A C A A C A A T A A T G

Fig. 4

Fig. 5

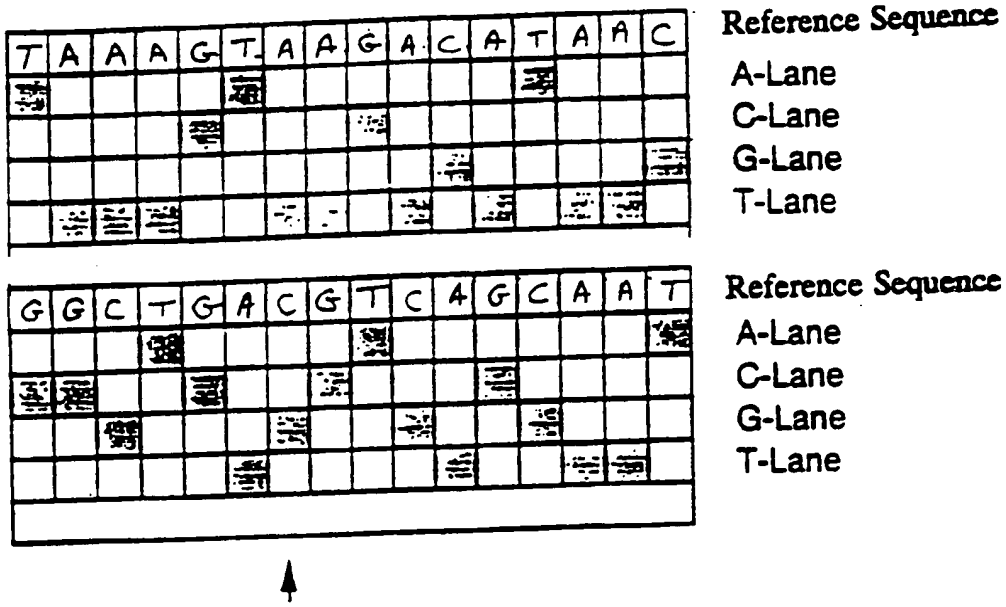

FIG. 5 : Tiled Array with Probes for the Detection of Point Mutations

3'-CCGACTACAGTCGTT
3'-CCGACTCCAGTCGTT
3'-CCGACTGCAGTCGTT
3'-CCGACTTCAGTCGTT

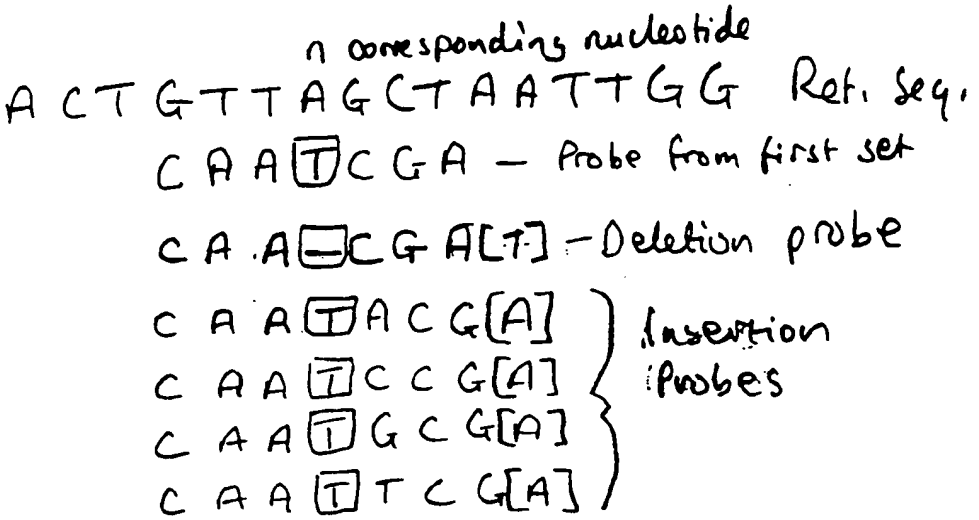
n corresponding nucleotide
A C T G T T A G C T A A T T G G Ref. Seq.
C A A T C G A – Probe from first set
C A A – C G A [T] – Deletion probe
C A A T A C G [A]
C A A T C C G [A]
C A A T G C G [A]
C A A T T C G [A]
Insertion Probes

Fig. 6

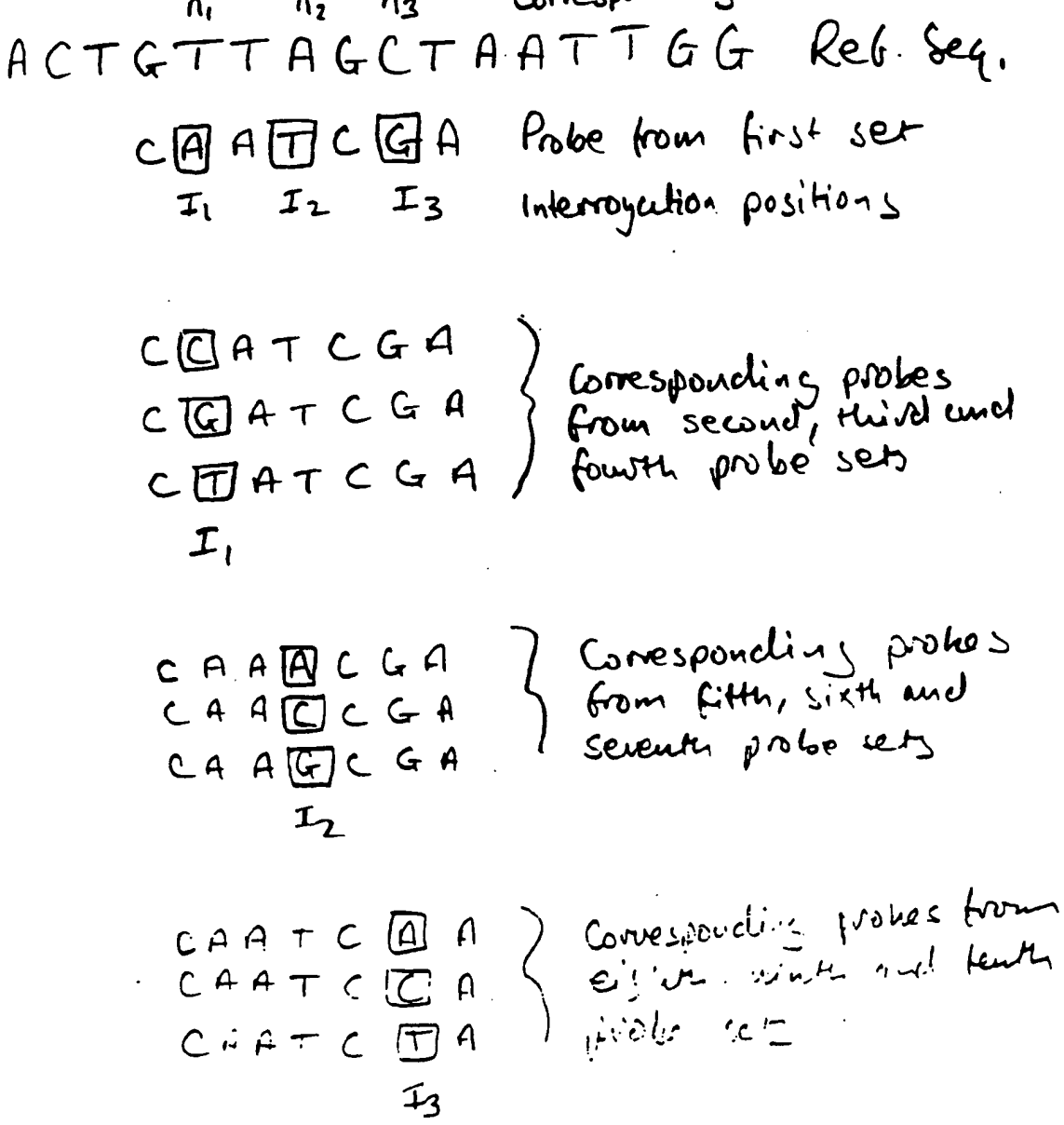
n1 n2 n3 Corresponding nucleotides
ACTGTTAGCTAATTGG Ref. Seq.
CAATCGA Probe from first set
I1 I2 I3 Interrogation positions
CCATCGA
CGATCGA
CTATCGA
I1
Corresponding probes from second, third and fourth probe sets
CAAACGA
CAACCGA
CAAGCGA
I2
Corresponding probes from fifth, sixth and seventh probe sets
CAATCAA
CAATCCA
CAATCTA
I3
Corresponding probes from eighth, ninth and tenth probe sets

Fig. 7

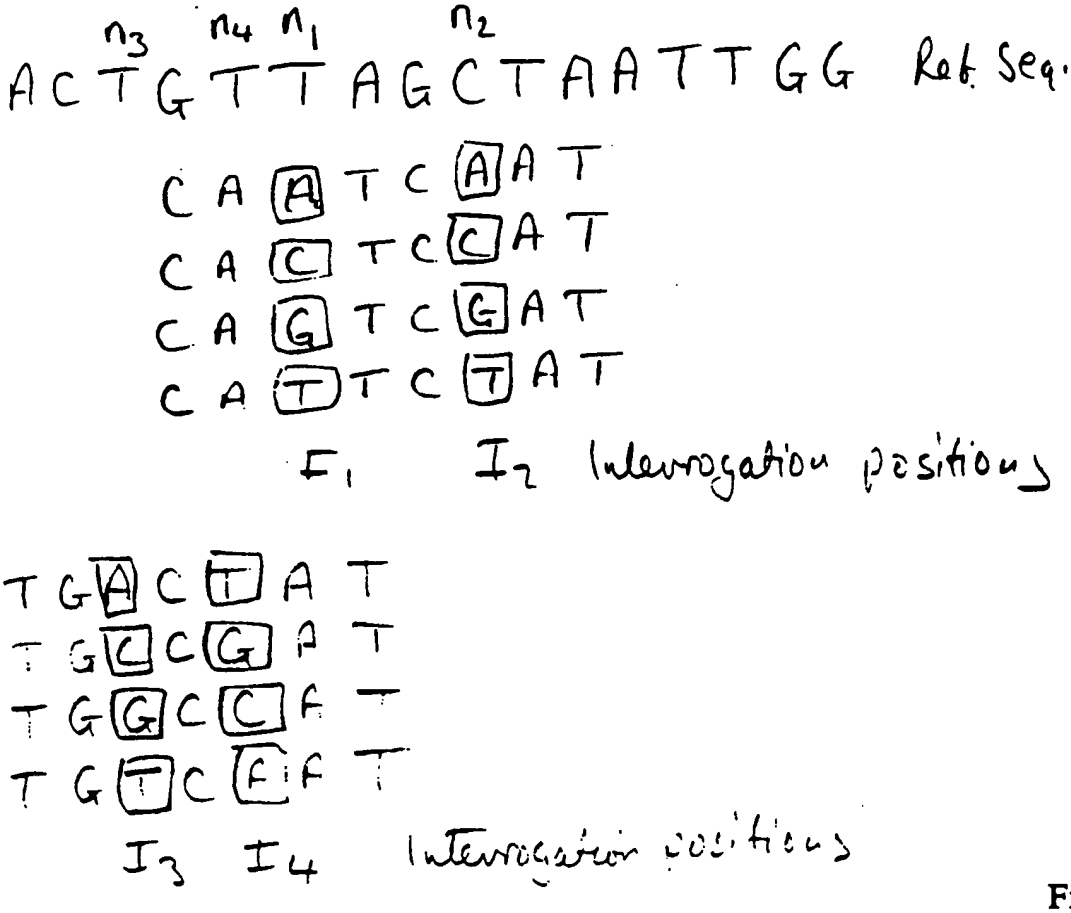
n3 n4 n1 n2
ACTGTTAGCTAATTGG Ref Seq.
CAATCAAT
CACTCCAT
CAGTCGAT
CATTCTAT
I1 I2 Interrogation positions
TGACTAT
TGCCGAT
TGGCCAT
TGTCFFT
I3 I4 Interrogation positions

Fig. 8

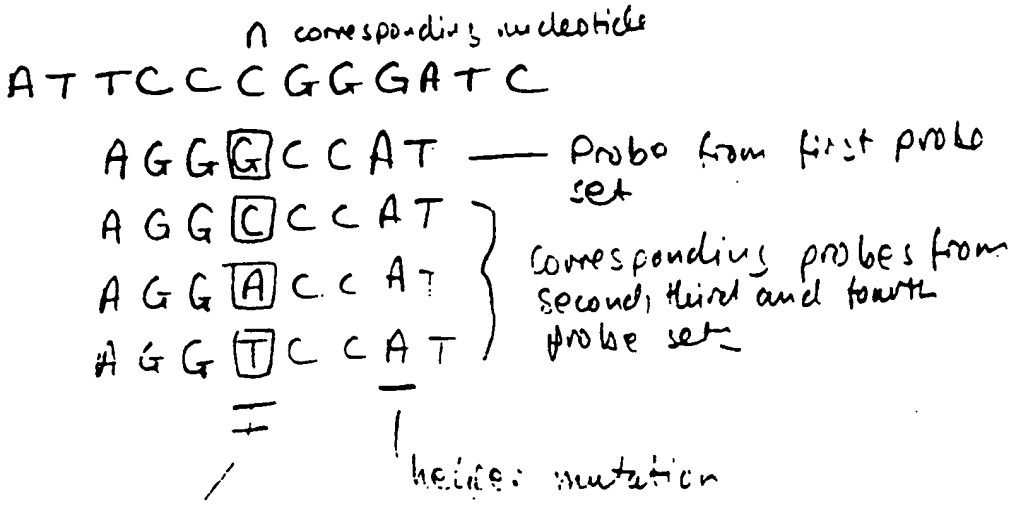
n corresponding nucleotide
ATTCCCGGGATC
AGGGCCAT — Probe from first probe set
AGGCCCAT
AGGACCAT
AGGTCCAT
Corresponding probes from second, third and fourth probe set
Interrogation position
heige: mutation

Fig. 9

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HV 407A 130 x 140

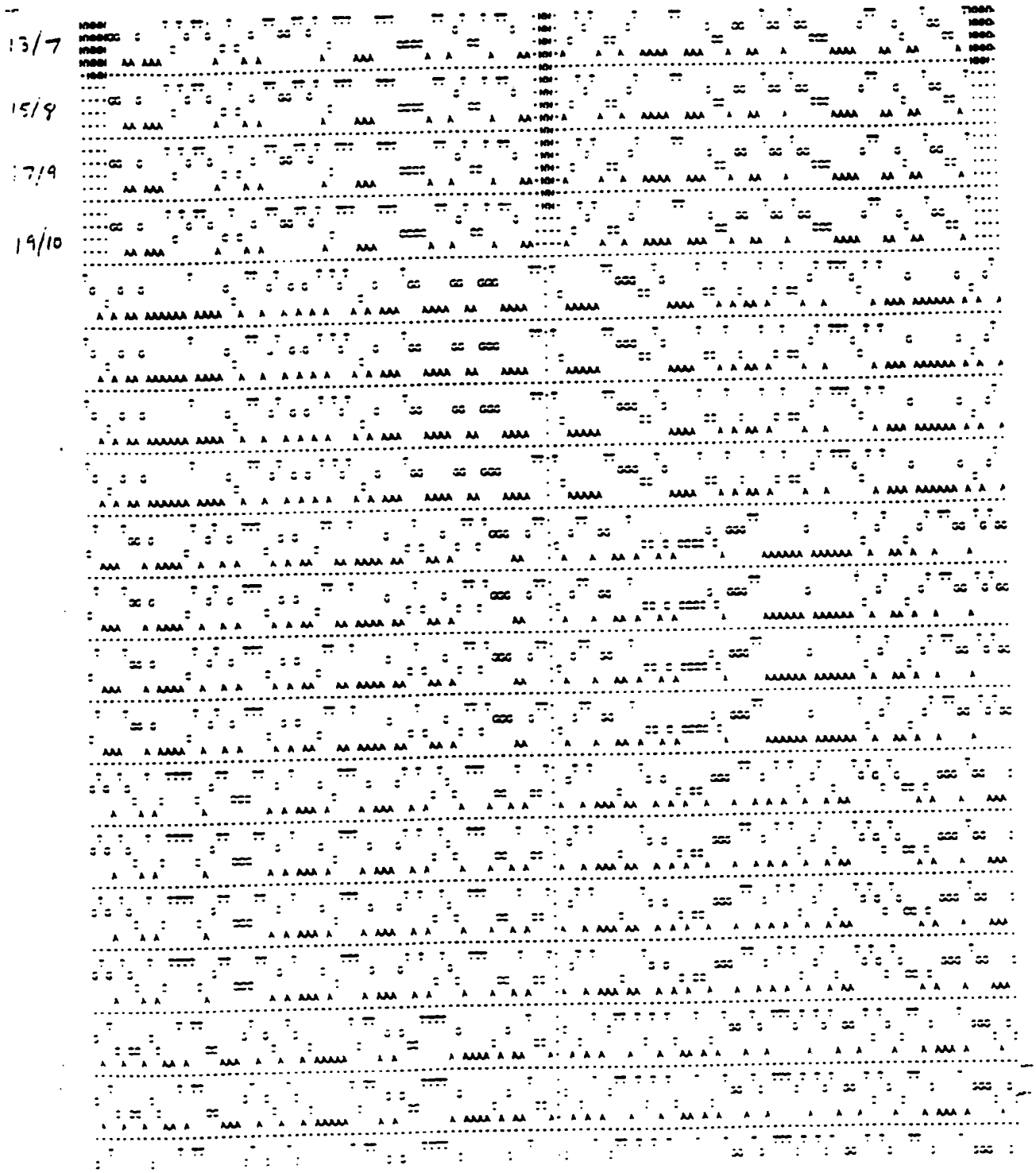

Fig. 10
Page 1 of 2

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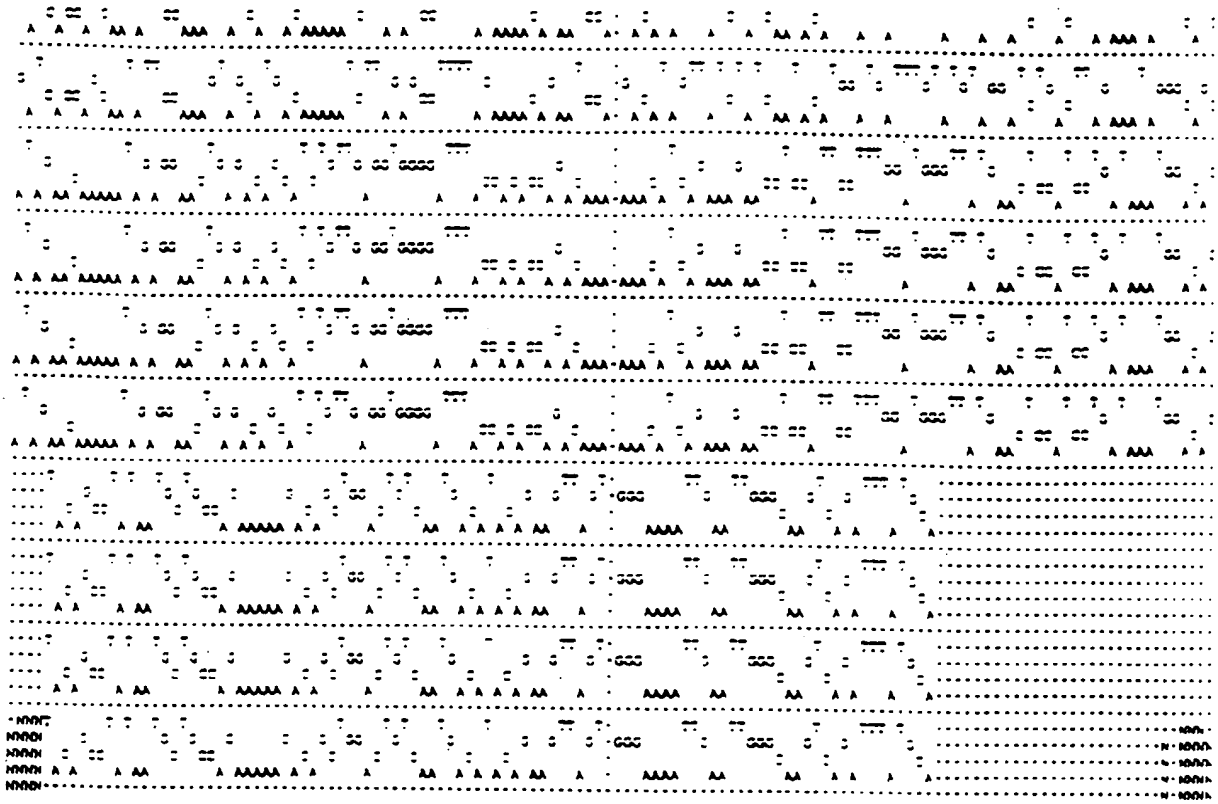
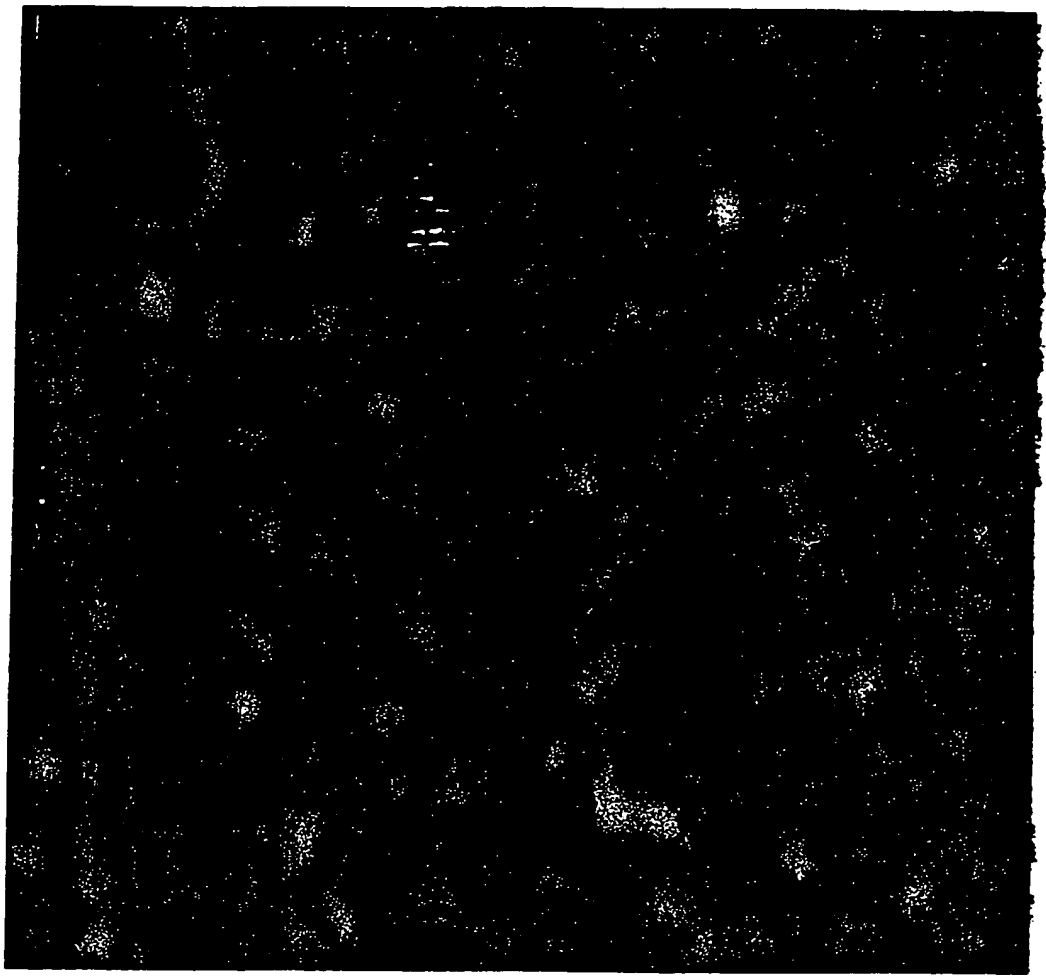


Fig. 10
Page 2 of 2



MC07060:

=407 wafer chip hybridized with fragmented pfol 19 RNA

Fig. 11

1177

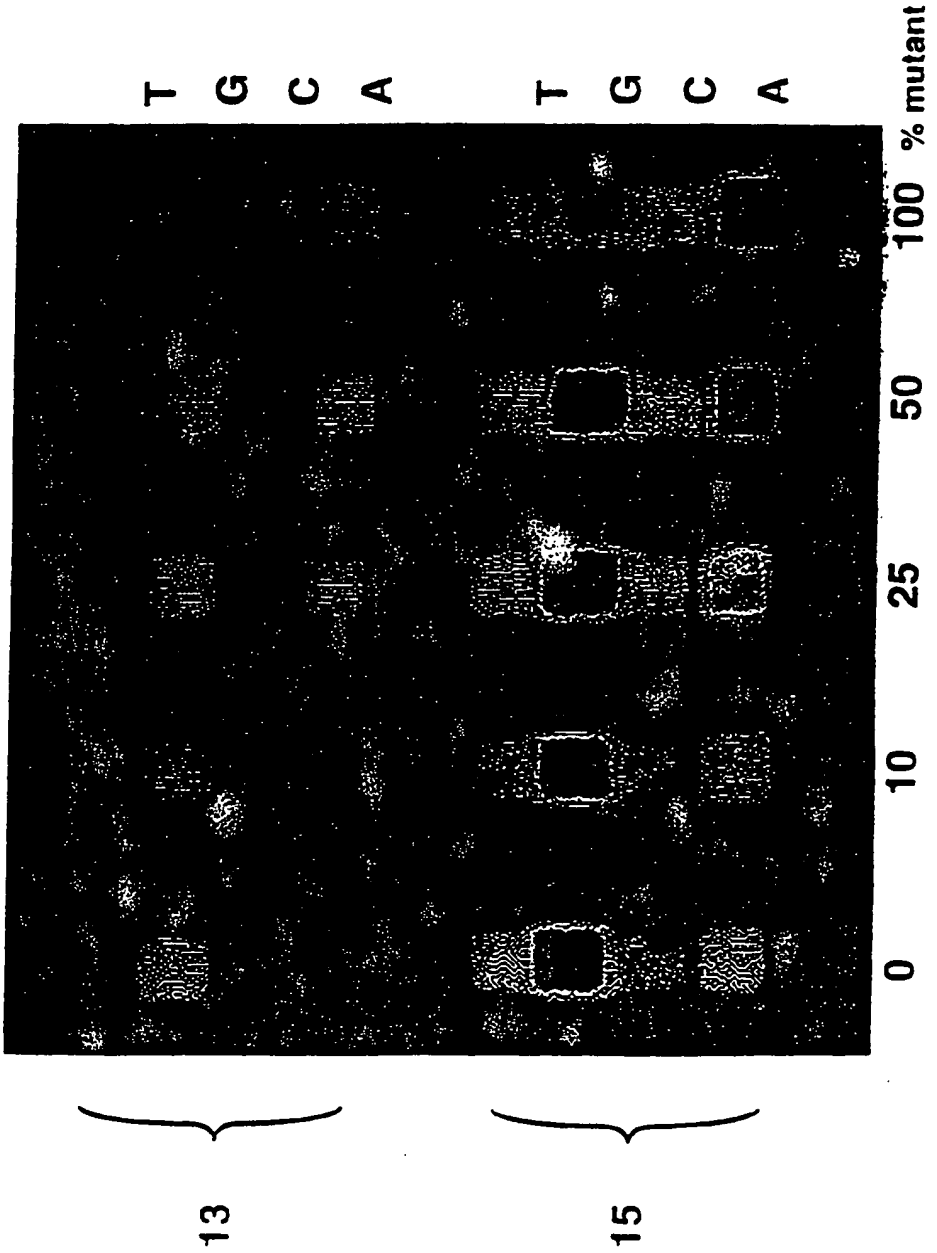
Figure 12
(Page 1 of 2)

Figure 12
(Page 2 of 2)

```
5'Fluorescein-AAAGAAAAAAGACAGTACTAAATGGAGAAAAT wildtype
PROBE 3'          tttttt•tgtcat          13mers
PROBE 3'        ctttttt•tgtcatg          15mers
PROBE 3'      tctttttt•tgtcatga          17mers
PROBE 3'    ttctttttt•tgtcatgat          19mers
5'Fluorescein-AAAGAAAAAAACAGTACTAAATGGAGAAAAT mutant
```

Fig. 13

Fig. 14



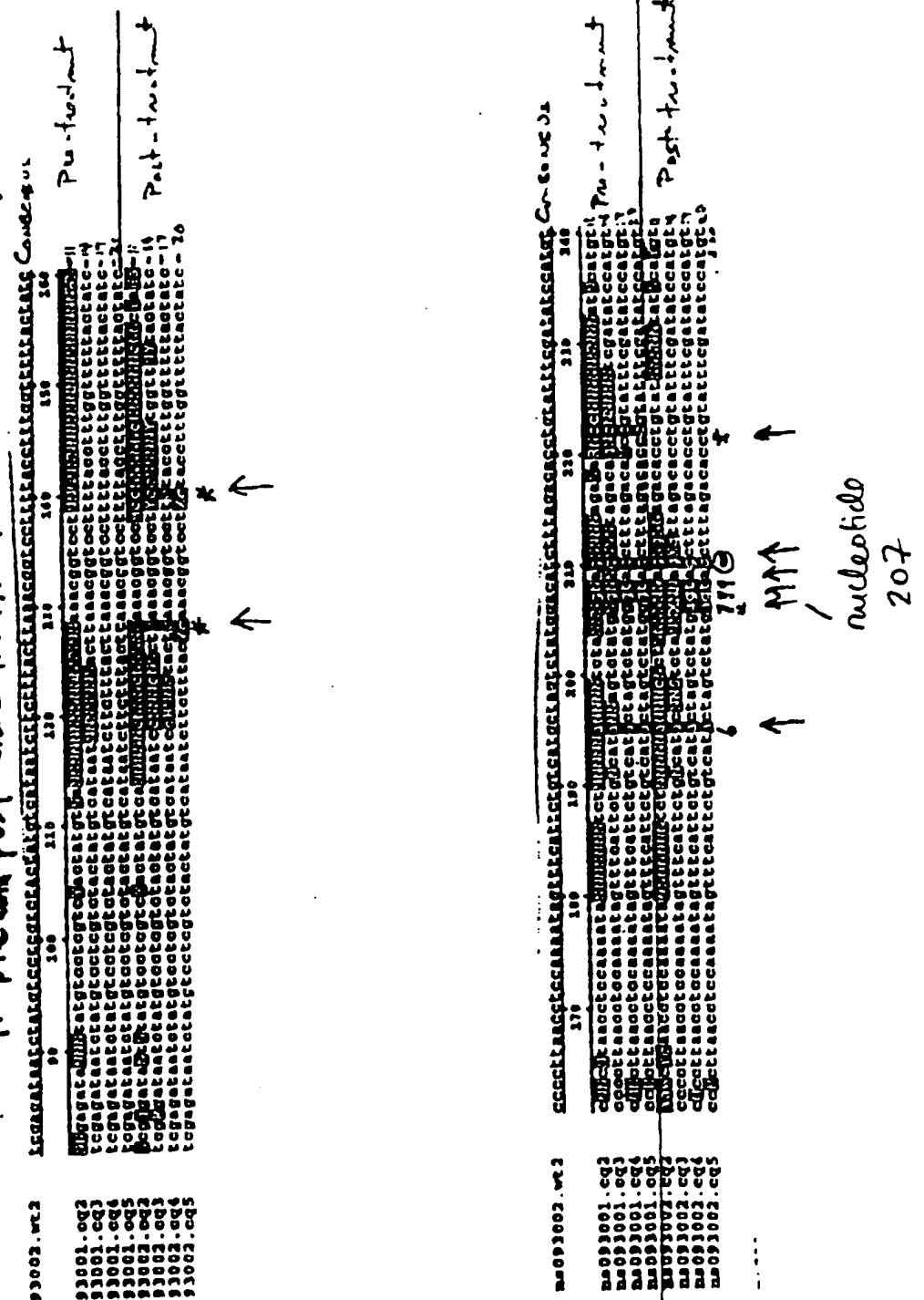

Genotyping of HIV-1 Protease Gene
In Pre and post-ddI treated Patients
Pre-treatment
Post-treatment
Post-treatment
nucleotide
207

Fig. 15

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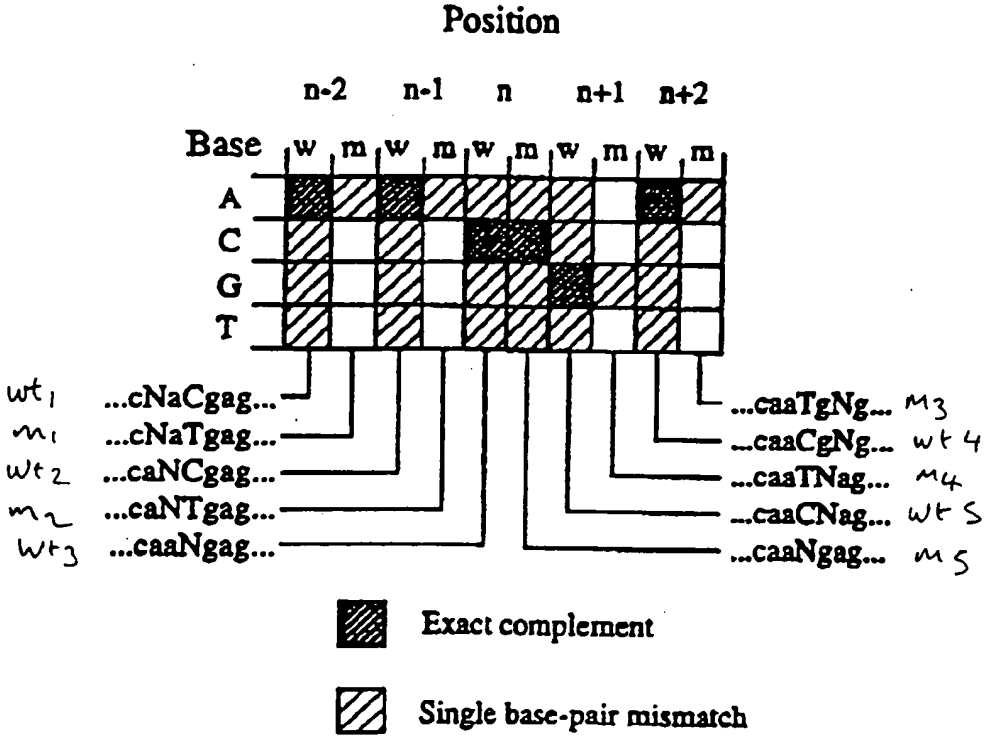
Array Design for the R553X Point Mutation

Wild-Type Pattern



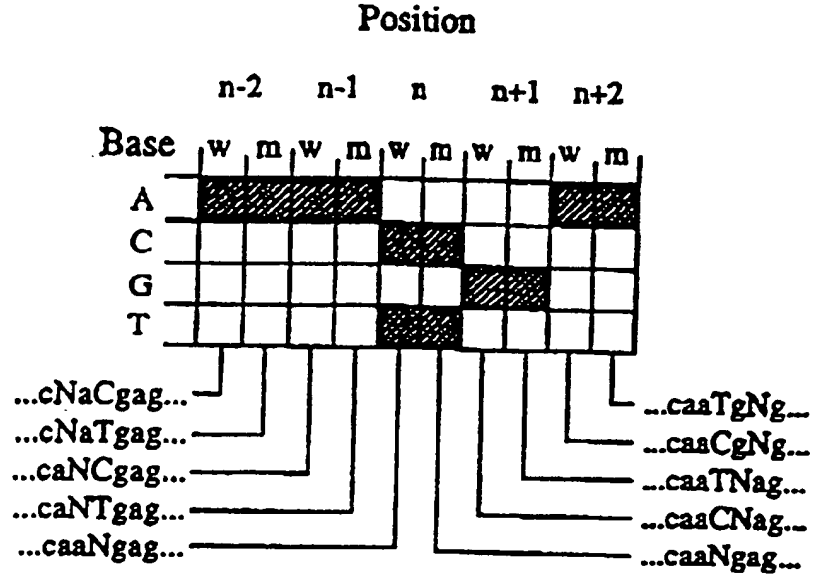
Wild-Type Sequence: 5'-AGGTCAA**C**GAGCAA-3'

Mutant Sequence: 5'-AGGTCAA**T**GAGCAA-3'

Fig. 16

Array Design for the R553X Point Mutation

Heterozygote Pattern



Wild-Type Sequence: 5'-AGGTCAACGAGCAA-3'

Mutant Sequence: 5'-AGGTCAATGAGCAA-3'

Fig. 17

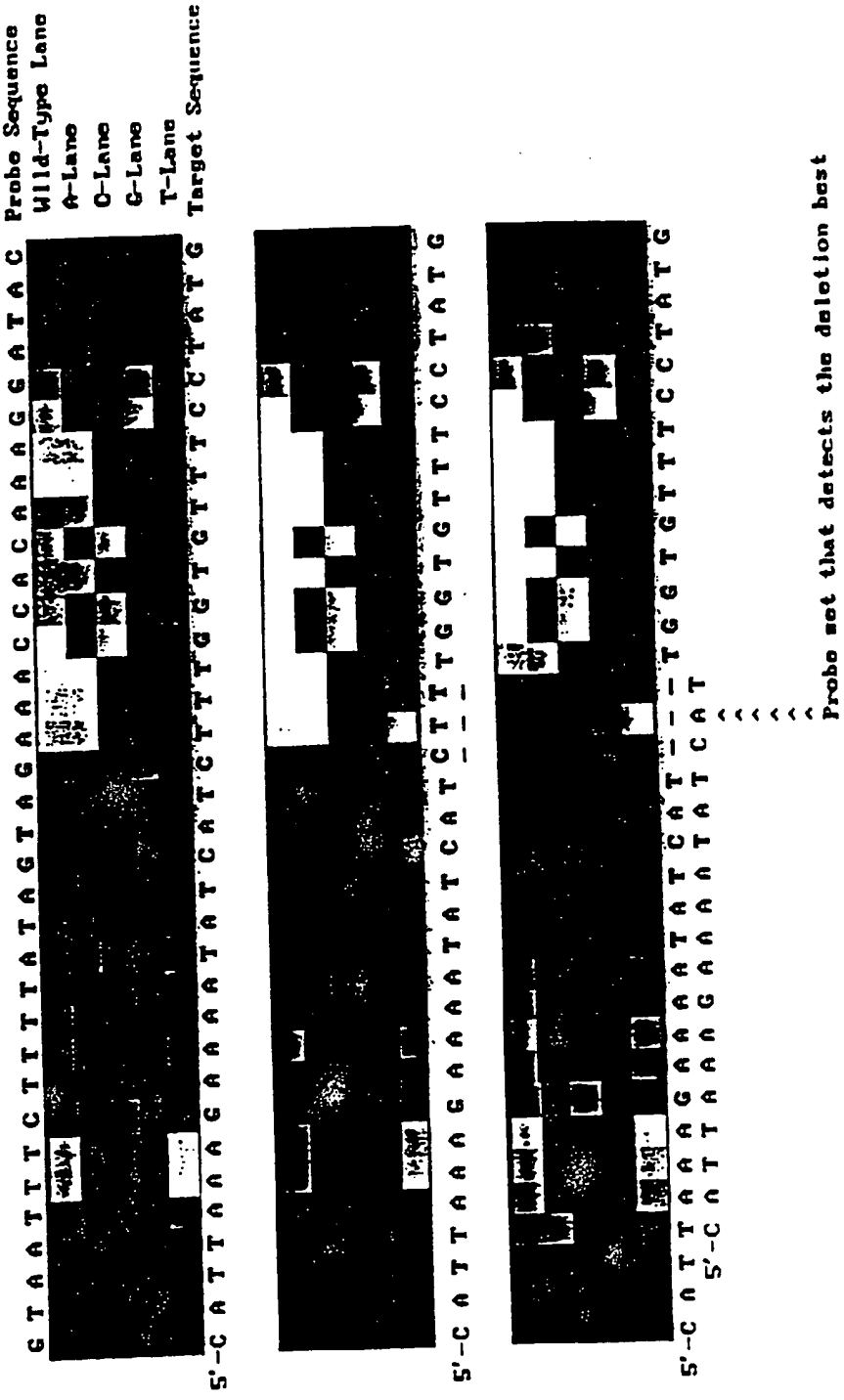

Probe Sequence
Wild-Type Lane
A-Lane
C-Lane
G-Lane
T-Lane
Target Sequence
5'-CATTAAAGAAAAATATCATCTTTGGTGTTTCCTATG
5'-CATTAAAGAAAAATATCATCTTTGGTGTTTCCTATG
5'-CATTAAAGAAAAATATCAT---TGGTGTTTCCTATG
<<<<<<<
Probe set that detects the deletion best
A
B
C

Fig. 18

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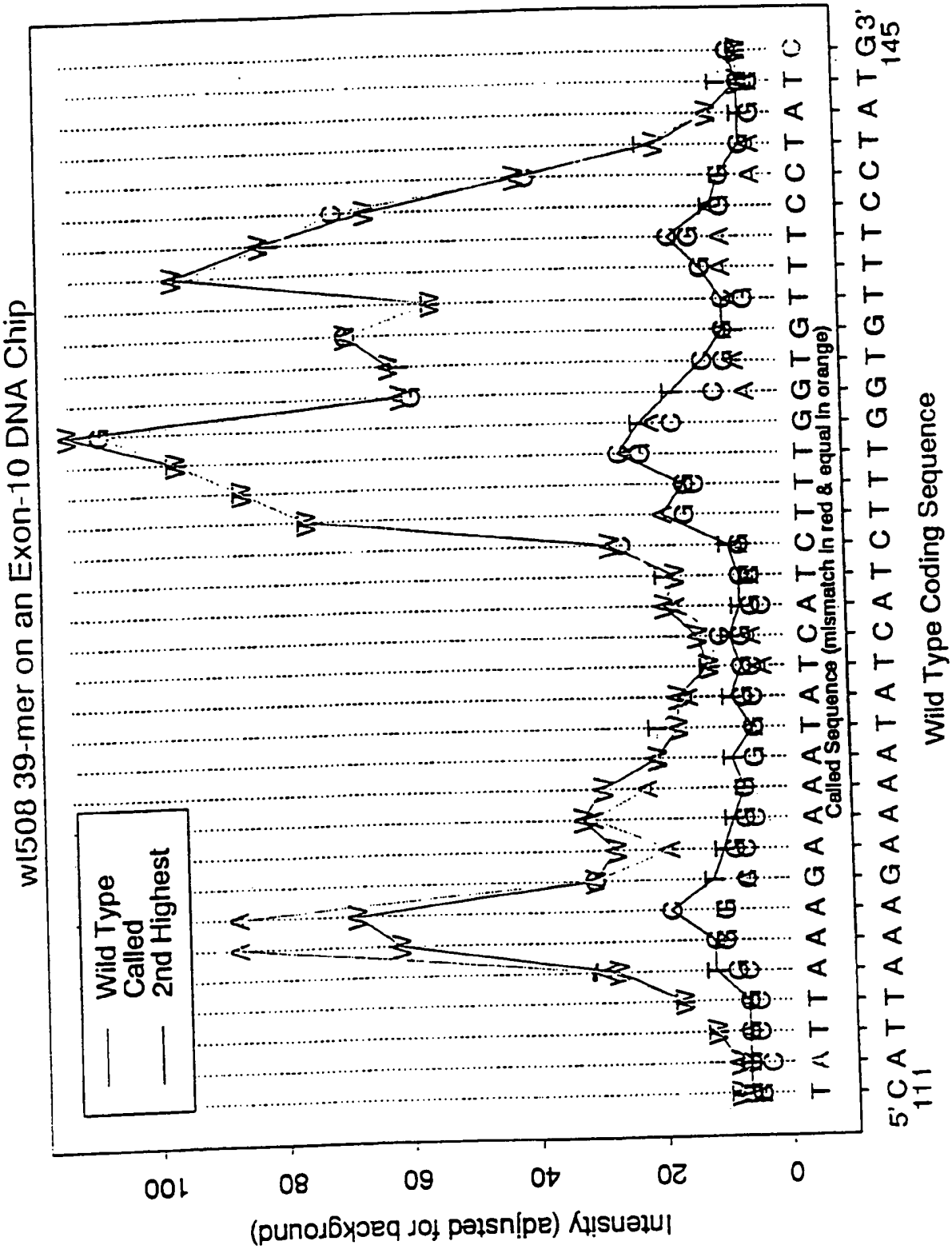

Fig. 19
Page 1 of 3

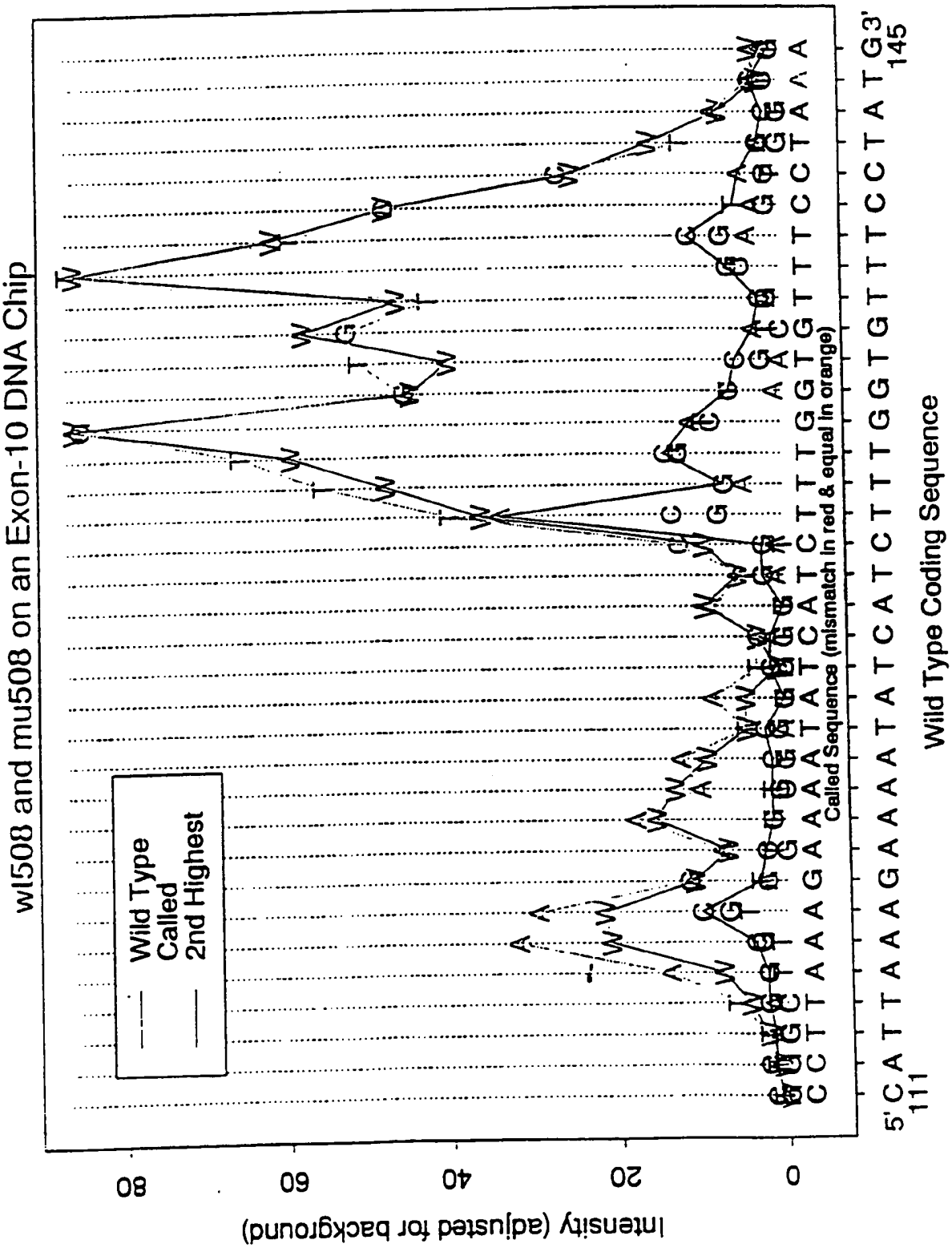

Fig. 19
Page 2 of 3

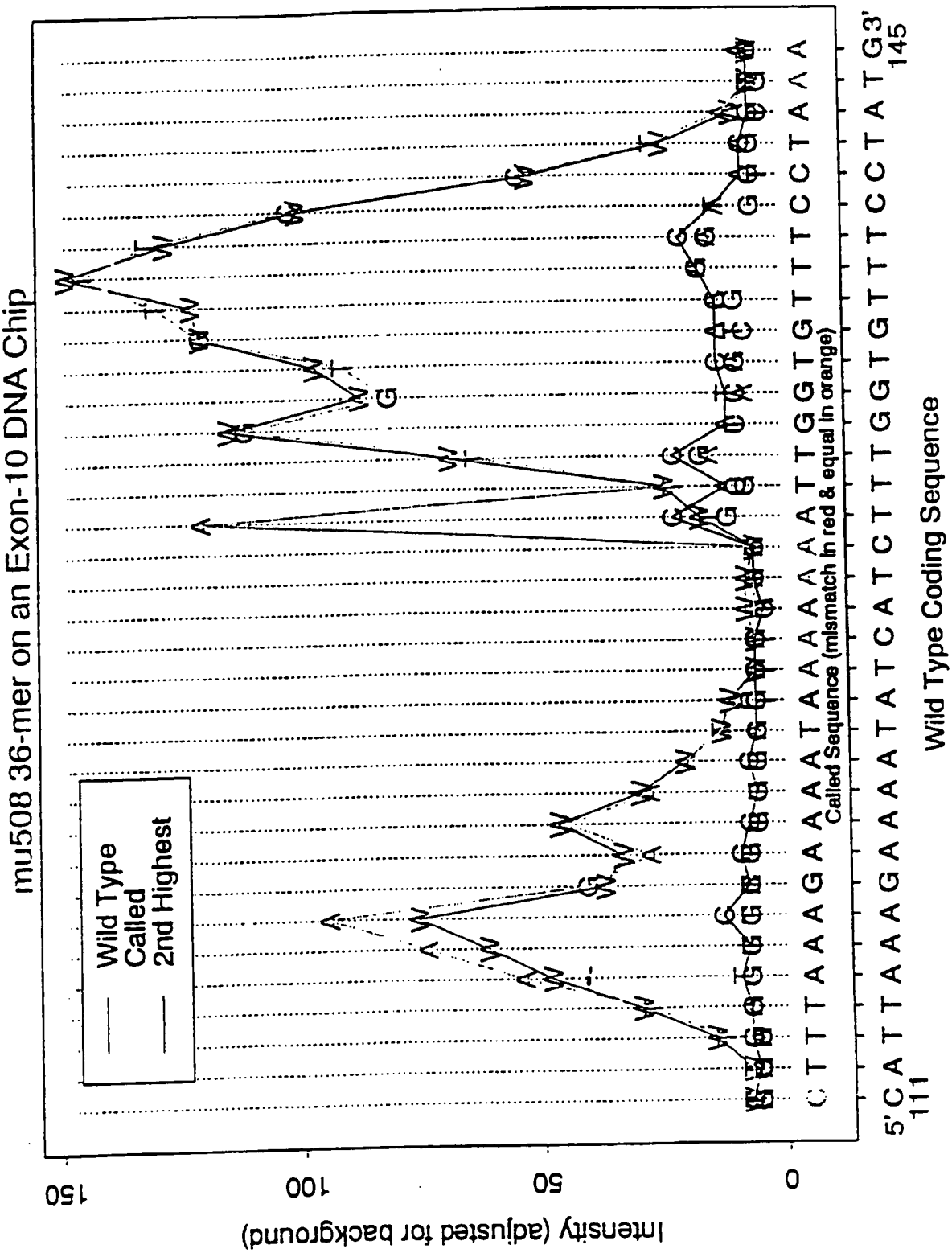

Fig. 19
Page 3 of 3

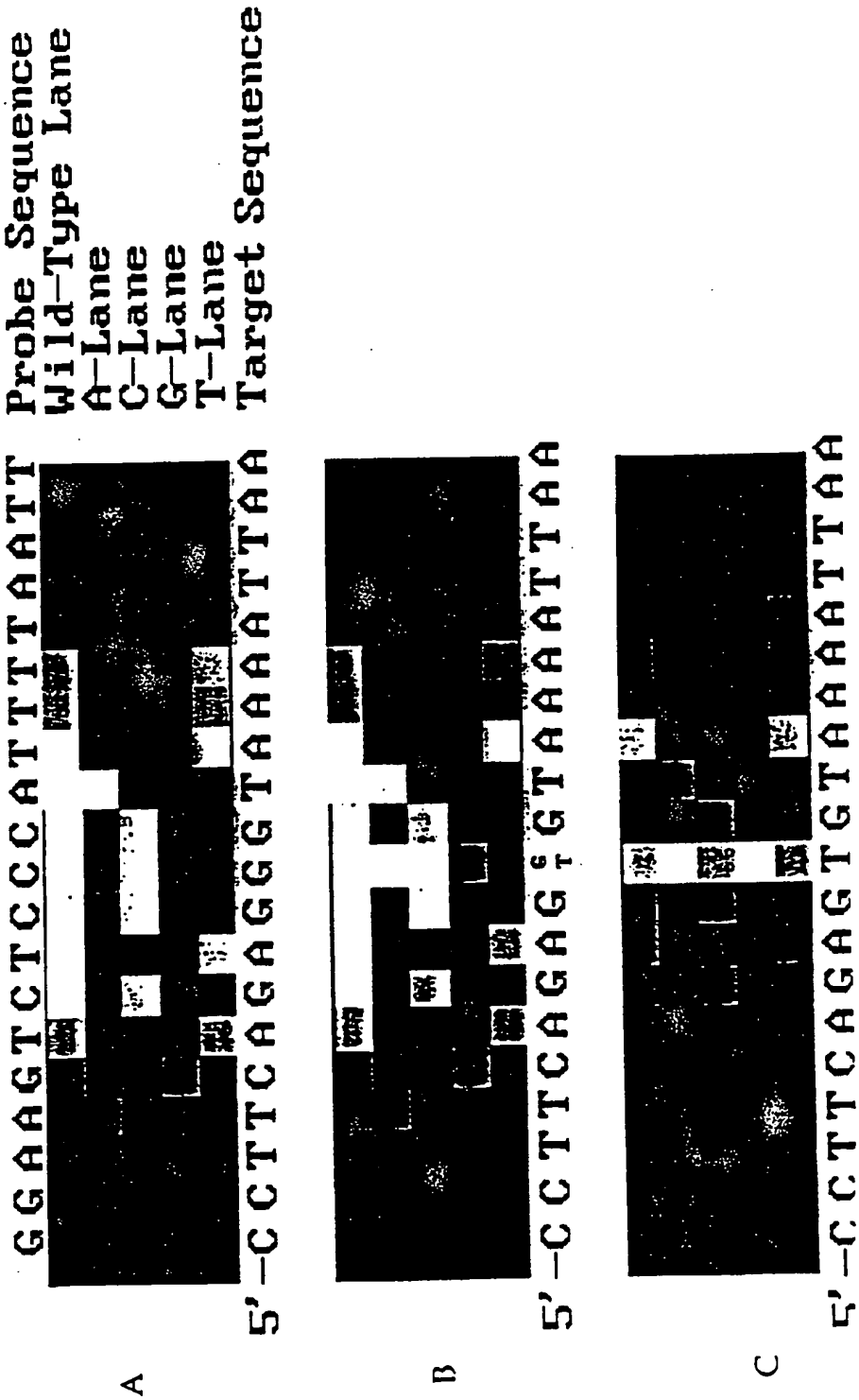
Probe Sequence
Wild-Type Lane
A-Lane
C-Lane
G-Lane
T-Lane
Target Sequence
GGAAGTCTCCCATTTAATT
5'-CCTTCAGAGGGTAAAATTAA
A
5'-CCTTCAGAGTGTAAAATTAA
B
5'-CCTTCAGAGTGTAAAATTAA
C

Fig. 20

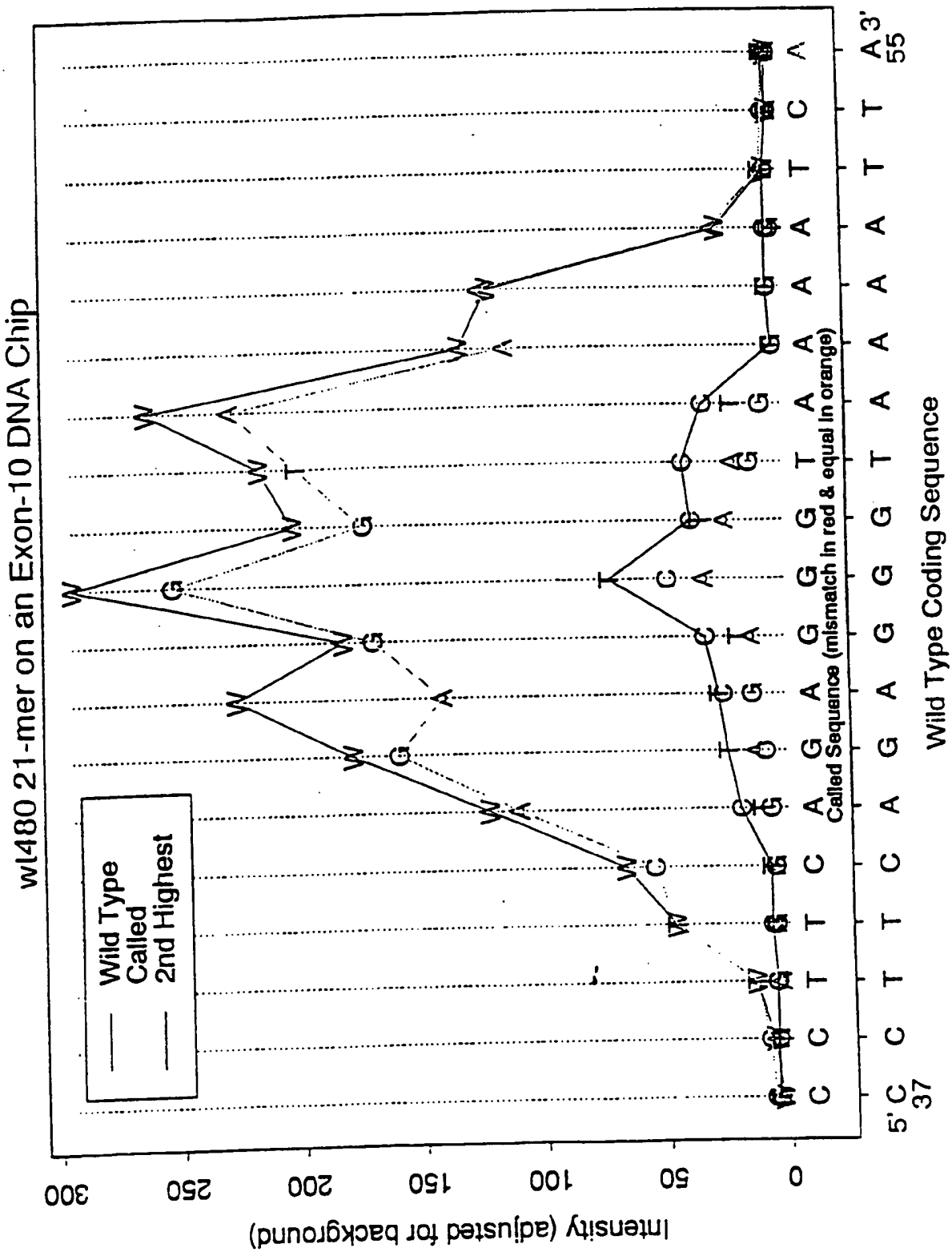

Fig. 21
Page 1 of 3

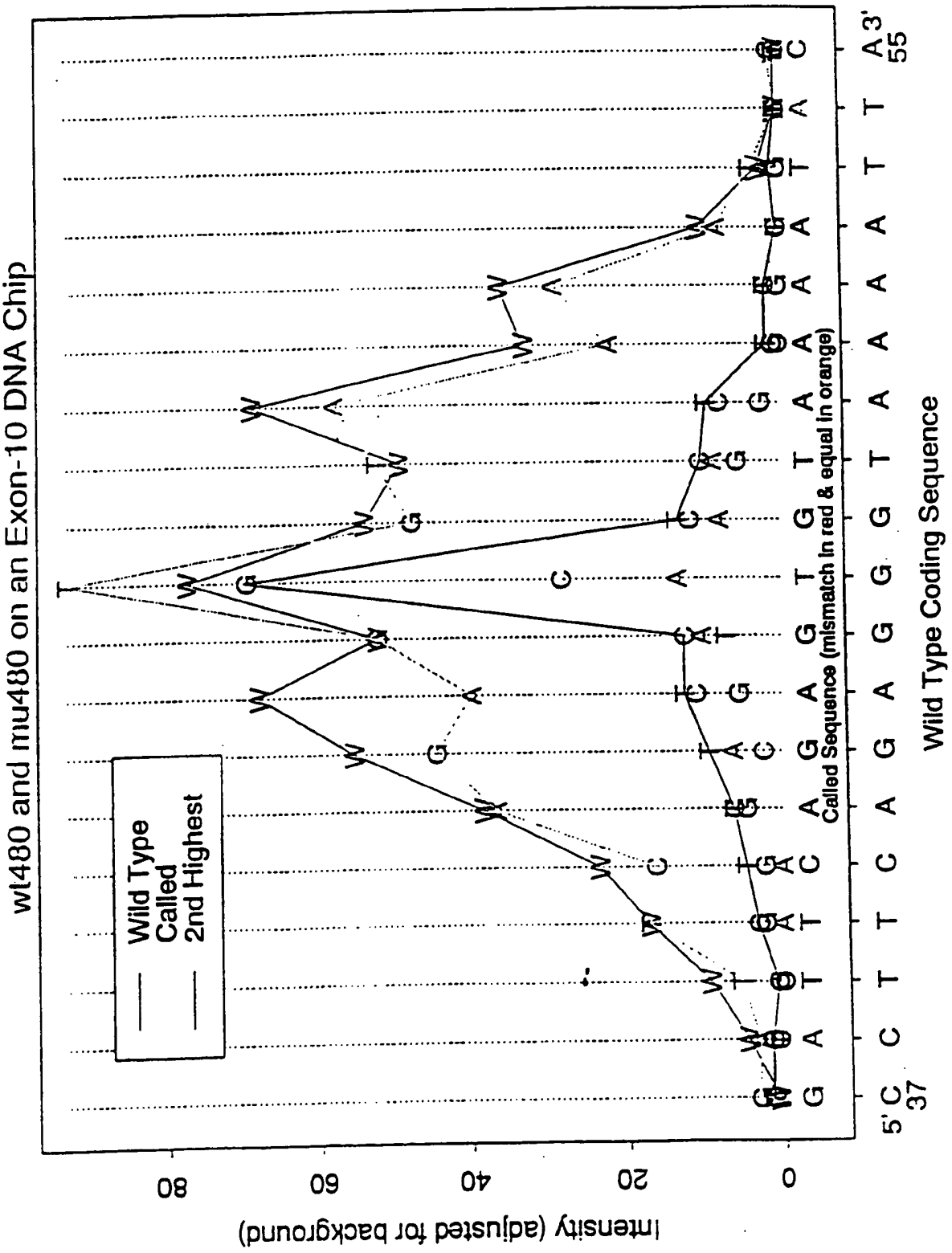

Fig. 21
Page 2 of 3

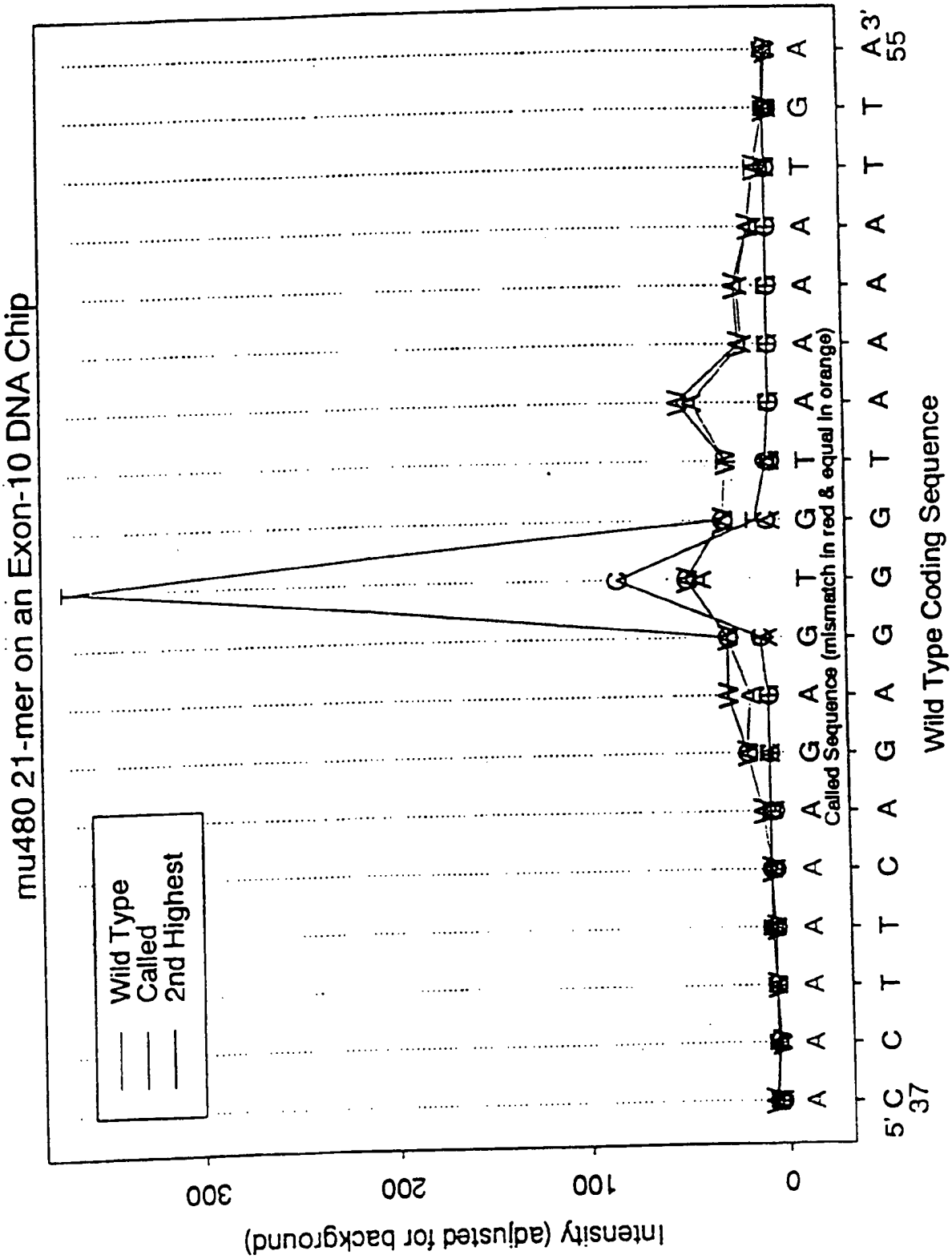

Fig. 21
Page 3 of 3

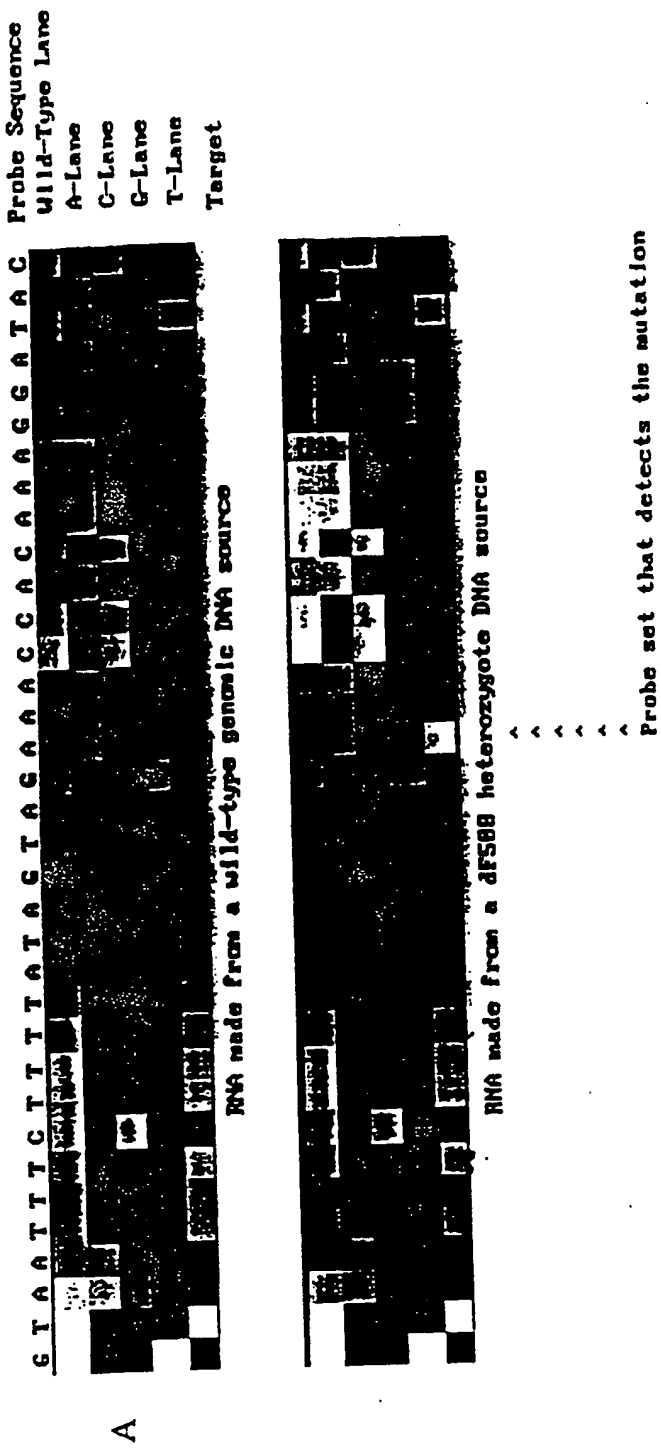
Probe Sequence
Wild-Type Lane
A-Lane
C-Lane
G-Lane
T-Lane
Target
GTAATTTCTTTTATAGTAGAAACCACAAAAGGATAC
RNA made from a wild-type genomic DNA source
RNA made from a dF508 heterozygote DNA source
Probe set that detects the mutation
A

Fig. 22

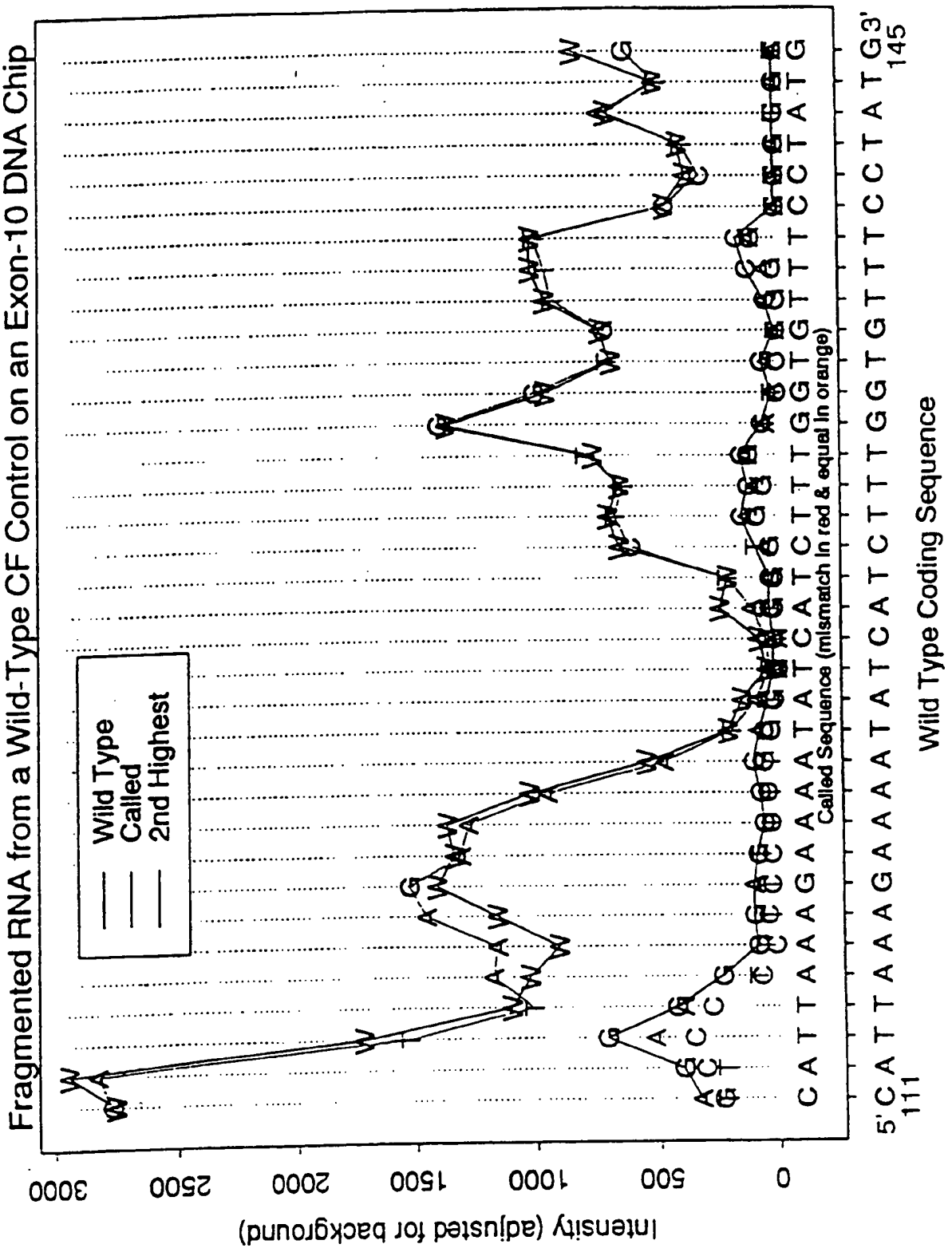

Fig. 23
Page 1 of 2

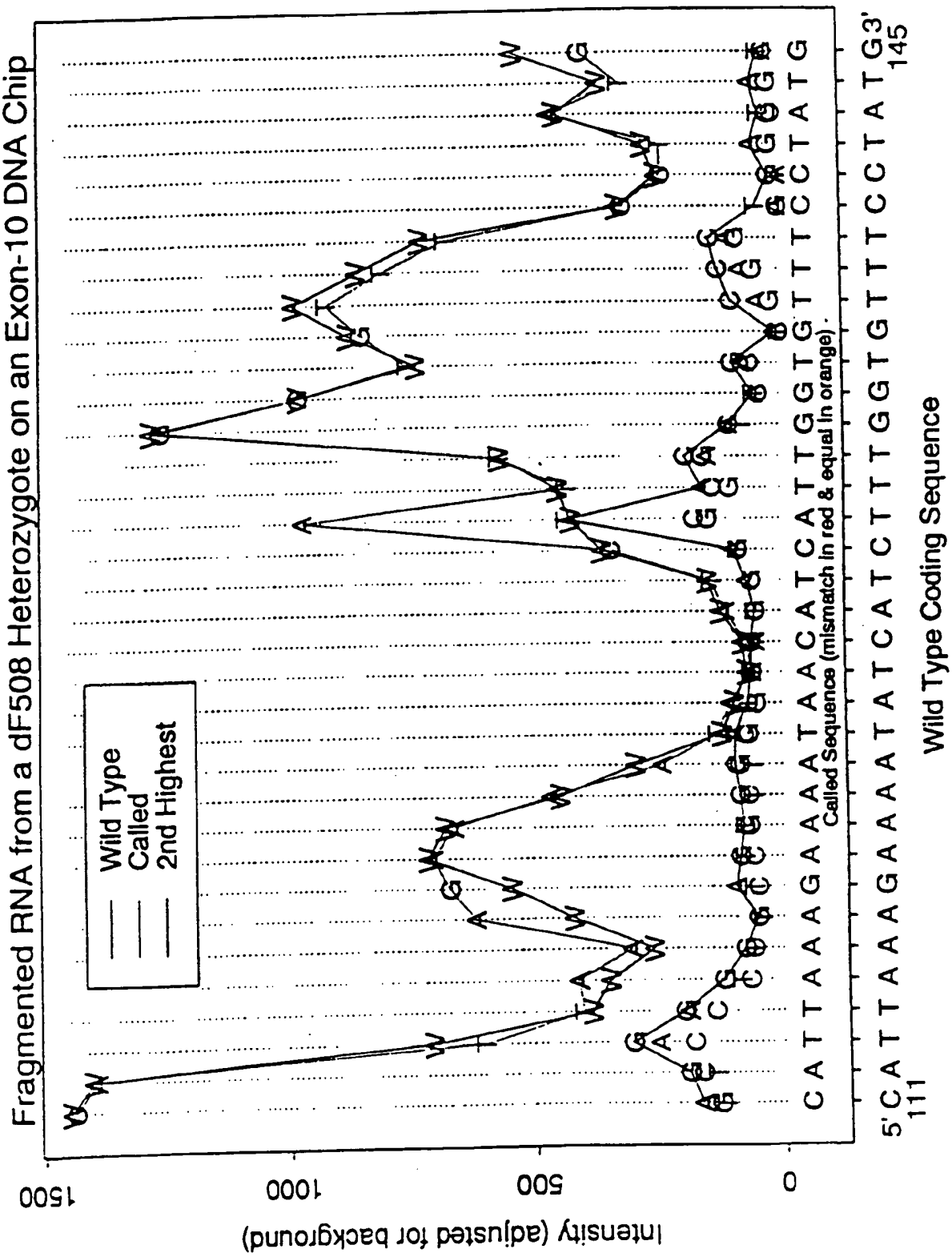
Fragmented RNA from a dF508 Heterozygote on an Exon-10 DNA Chip
Wild Type
Called
2nd Highest
Intensity (adjusted for background)
0
500
1000
1500
5'CATTTAAAGAAAATATCATCTTTGGTGTTTCCTATG3'
111
145
Called Sequence (mismatch in red & equal in orange)
Wild Type Coding Sequence

Fig. 23

A B

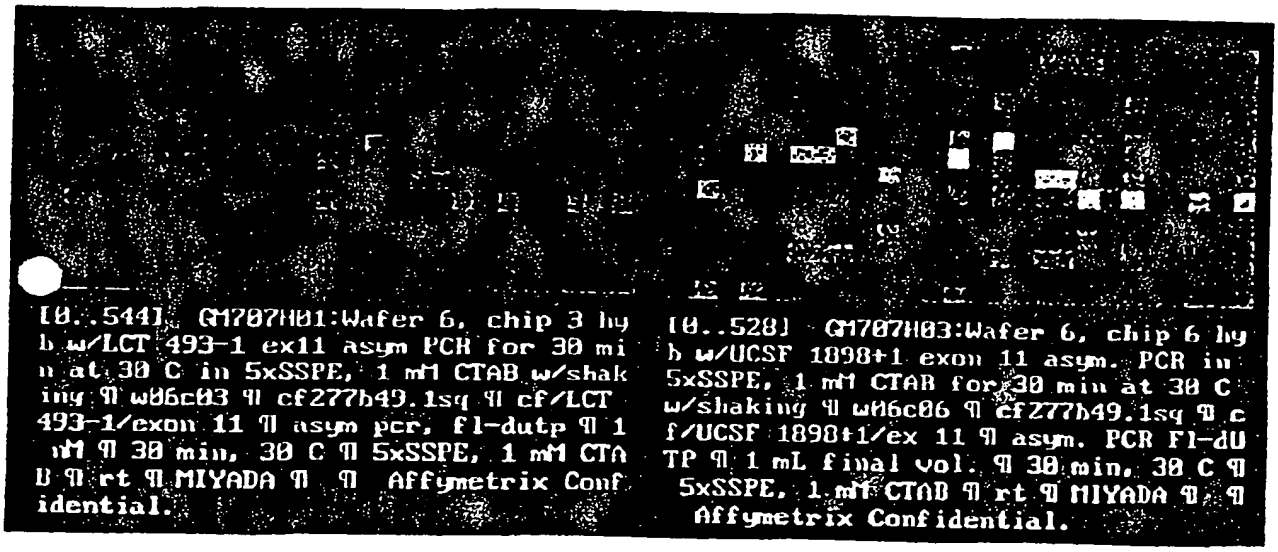
[0..544] GM707H01:Wafer 6, chip 3 hy b w/LCT 493-1 ex11 asym PCR for 30 mi n at 30 C in 5xSSPE, 1 mM CTAB w/shak ing ¶ w06c03 ¶ cf277b49.1sq ¶ cf/LCT 493-1/exon 11 ¶ asym pcr, fl-dutp ¶ 1 mM ¶ 30 min, 30 C ¶ 5xSSPE, 1 mM CTA B ¶ rt ¶ MIYADA ¶ ¶ Affymetrix Conf idential.
[0..528] GM707H03:Wafer 6, chip 6 hy b w/UCSF 1898+1 exon 11 asym. PCR in 5xSSPE, 1 mM CTAB for 30 min at 30 C w/shaking ¶ wH6c06 ¶ cf277b49.1sq ¶ c f/UCSF 1898+1/ex 11 ¶ asym. PCR Fl-dU TP ¶ 1 mL final vol. ¶ 30 min, 30 C ¶ 5xSSPE, 1 mM CTAB ¶ rt ¶ MIYADA ¶ ¶ Affymetrix Confidential.

Fig. 24

A

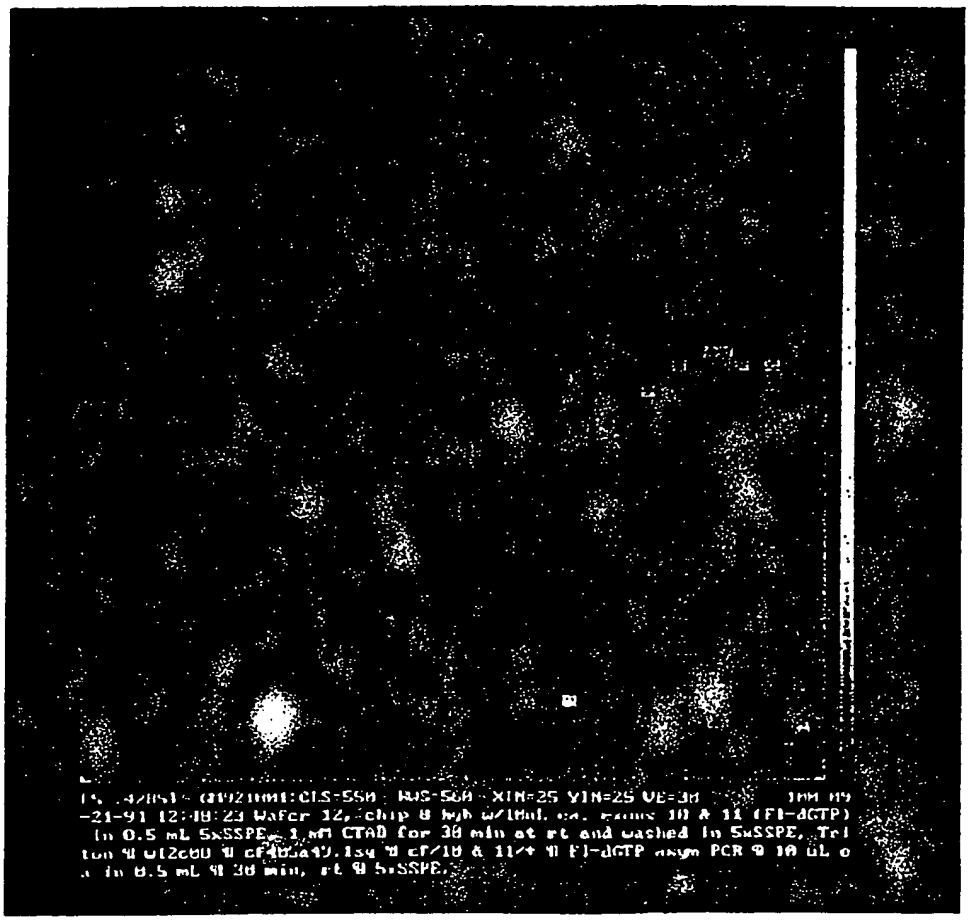

Fig. 25
Page 1 of 2

B

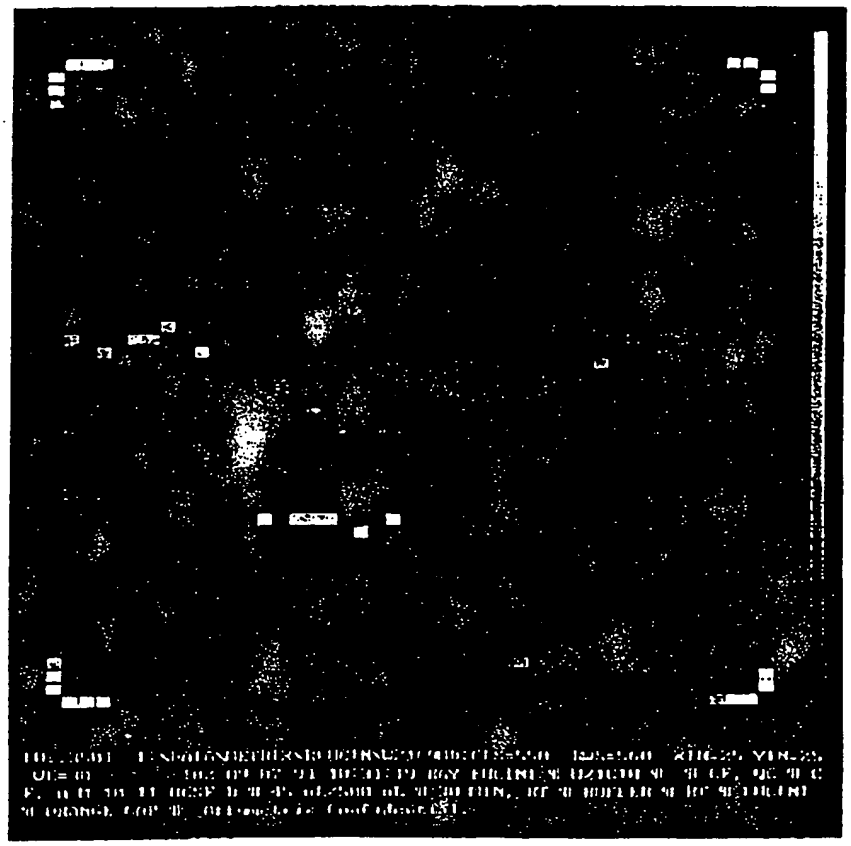

Fig. 25
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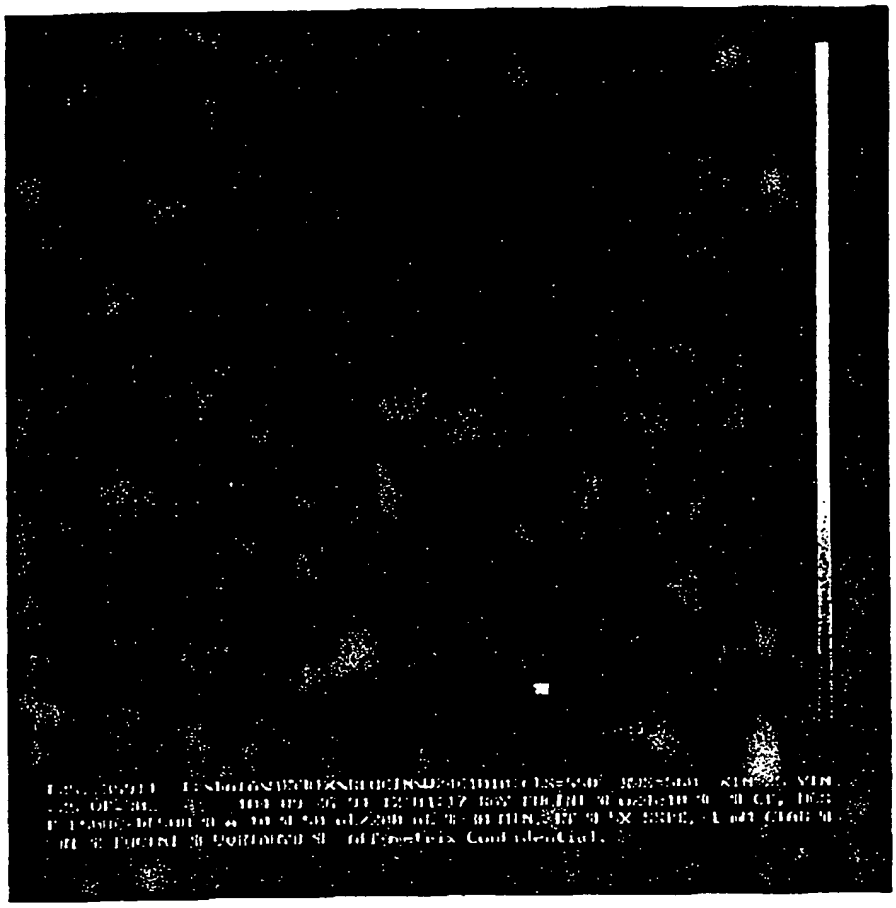


Fig. 26

P53 EXON 6 CODON 192 REGION: 12MER PROBES

								G	A	T	G	C	T	G	A	G	G	A	G				
0.														C	T	C	C	T	C	C	C	C	G	G	T
1.													A	C	T	C	C	T	C	C	C	C	G	G	
2.												G	A	C	T	C	C	T	C	C	C	C	G		
3.											C	G	A	C	T	C	C	T	C	C	C	C			
4.										A	C	G	A	C	T	C	C	T	C	C	C				
5.									T	A	C	G	A	C	T	C	C	T	C	C					
6.								C	T	A	C	G	A	C	T	C	C	T	C						
7.							T	C	T	A	C	G	A	C	T	C	C	T							
8.						T	T	C	T	A	C	G	A	C	T	C	C								
9.					A	T	T	C	T	A	C	G	A	C	T	C									
10.				T	A	T	T	C	T	A	C	G	A	C	T										
11.			C	T	A	T	T	C	T	A	C	G	A	C											
12.	C	C	T	A	T	T	C	T	A	C	G	A													

Fig. 27

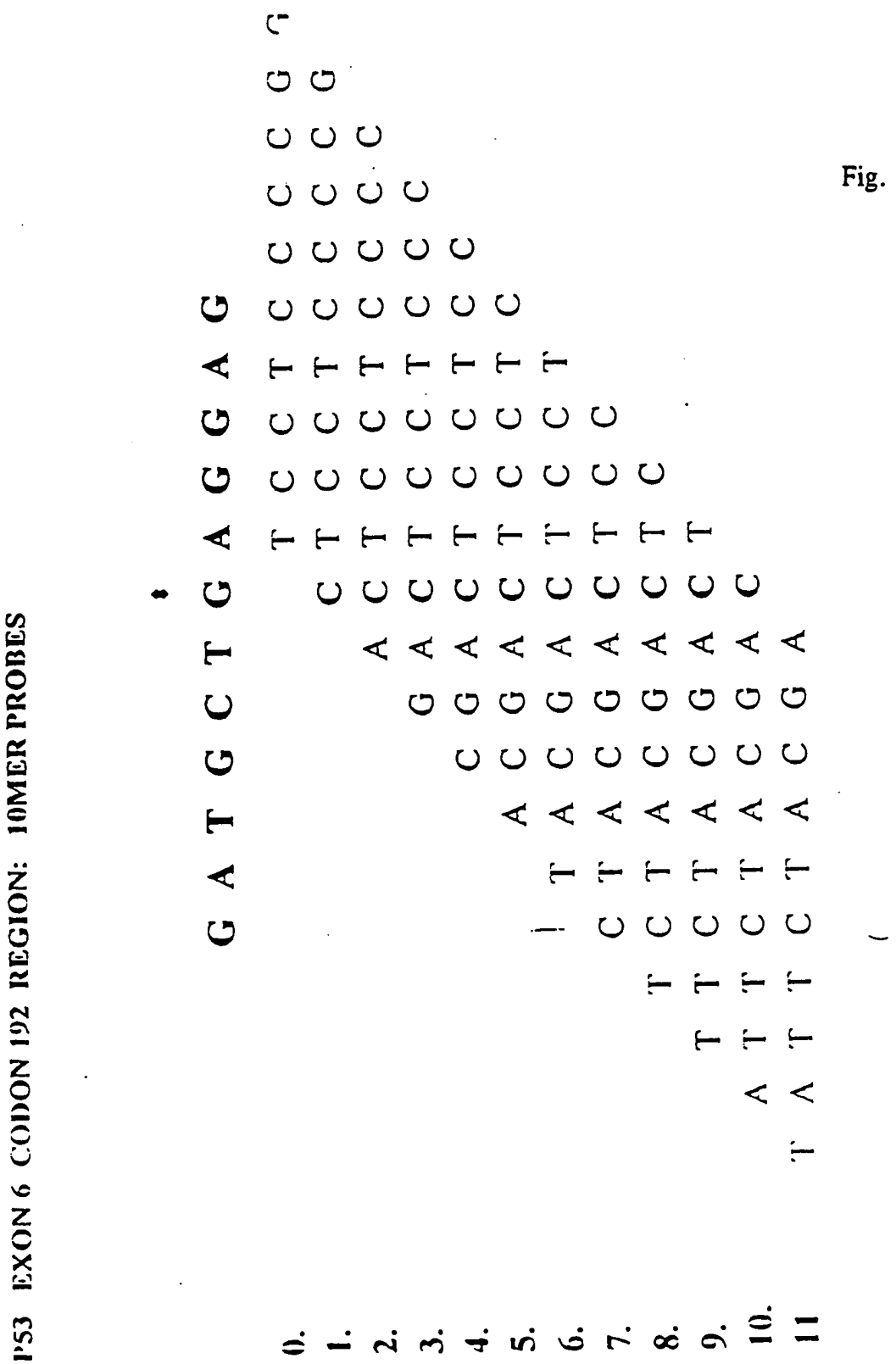
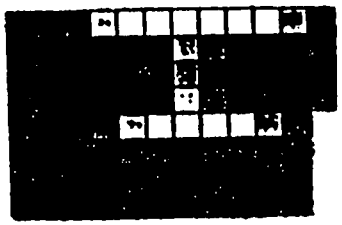

P53 EXON 6 CODON 192 REGION: 10MER PROBES
G A T G C T G A G G A G
0.
1.
2.
3.
4.
5.
6.
7.
8.
9.
10.
11.

Fig. 28

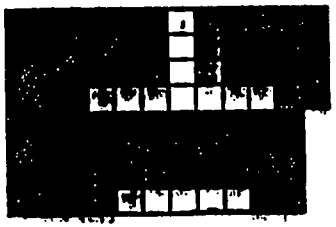
Detection of 12-mer One-Base Sustitution P53 Targets

Fig. 29

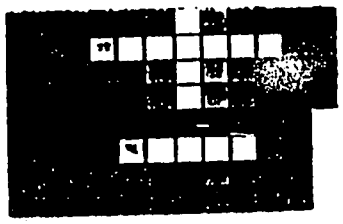
WT ("G" Substitution) Target 12-mer



"A Substitution 12-mer Target



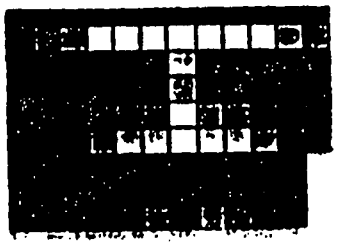
"T" Substitution Target 12-mer



"C"Substitution Target 12-mer

Fig. 31

4:1 Mixture of WT and "A" Substitution 12-mer Targets



Figs. 29 and 31

P53 EXON 6 CODON 192 REGION

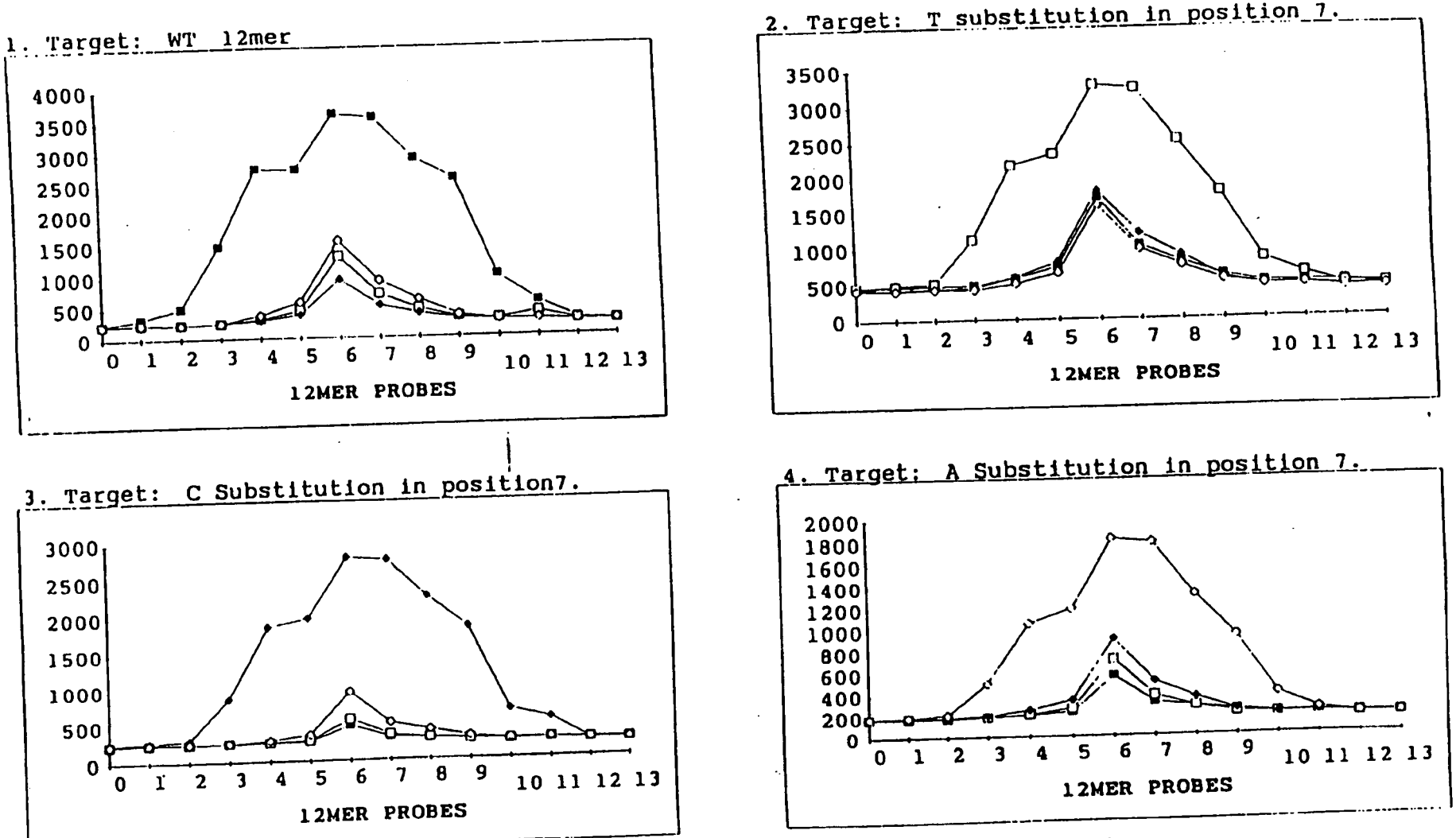


Fig. 30

P53 EXON 6 CODON 192 REGION

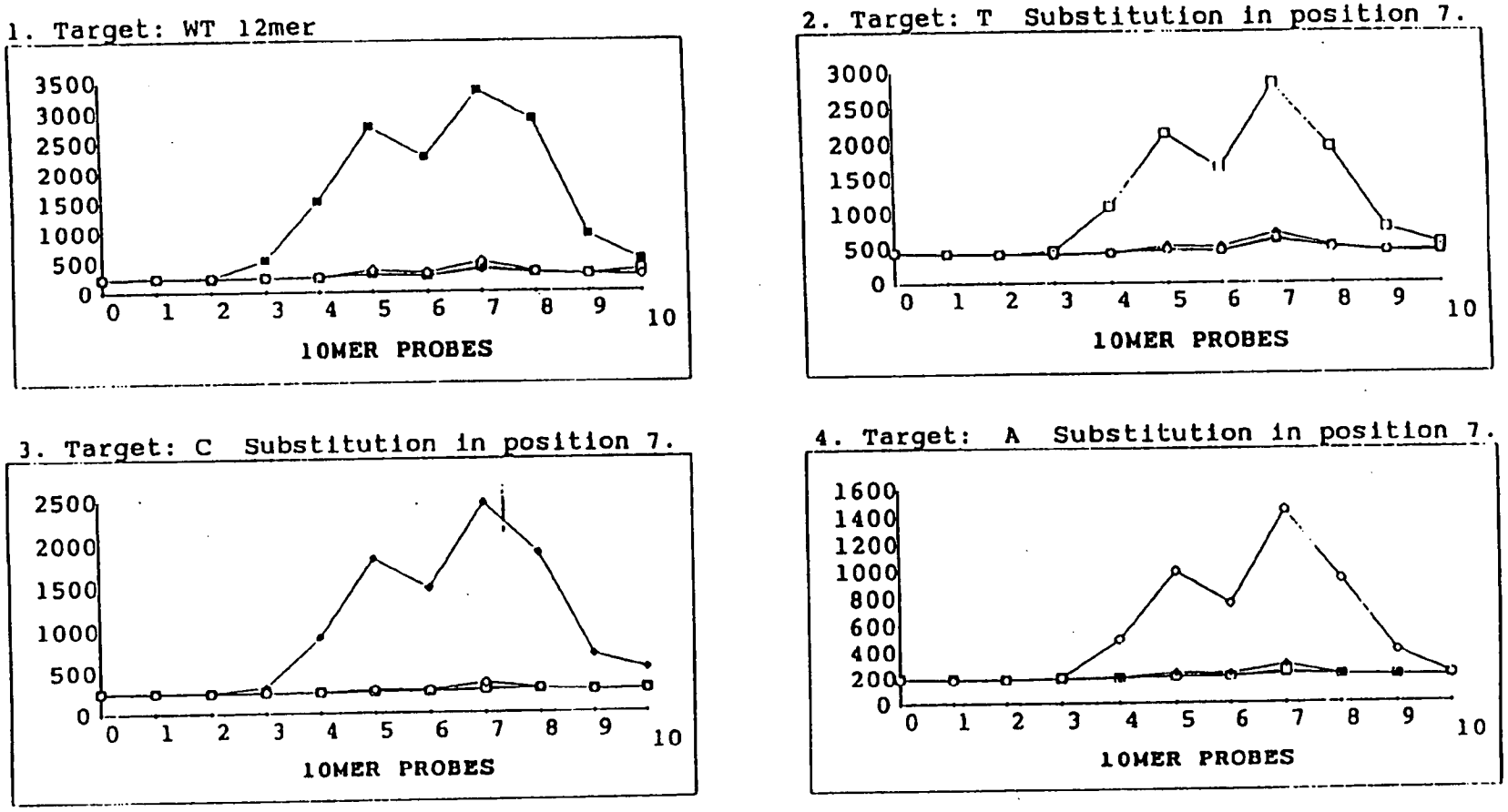


Fig. 32

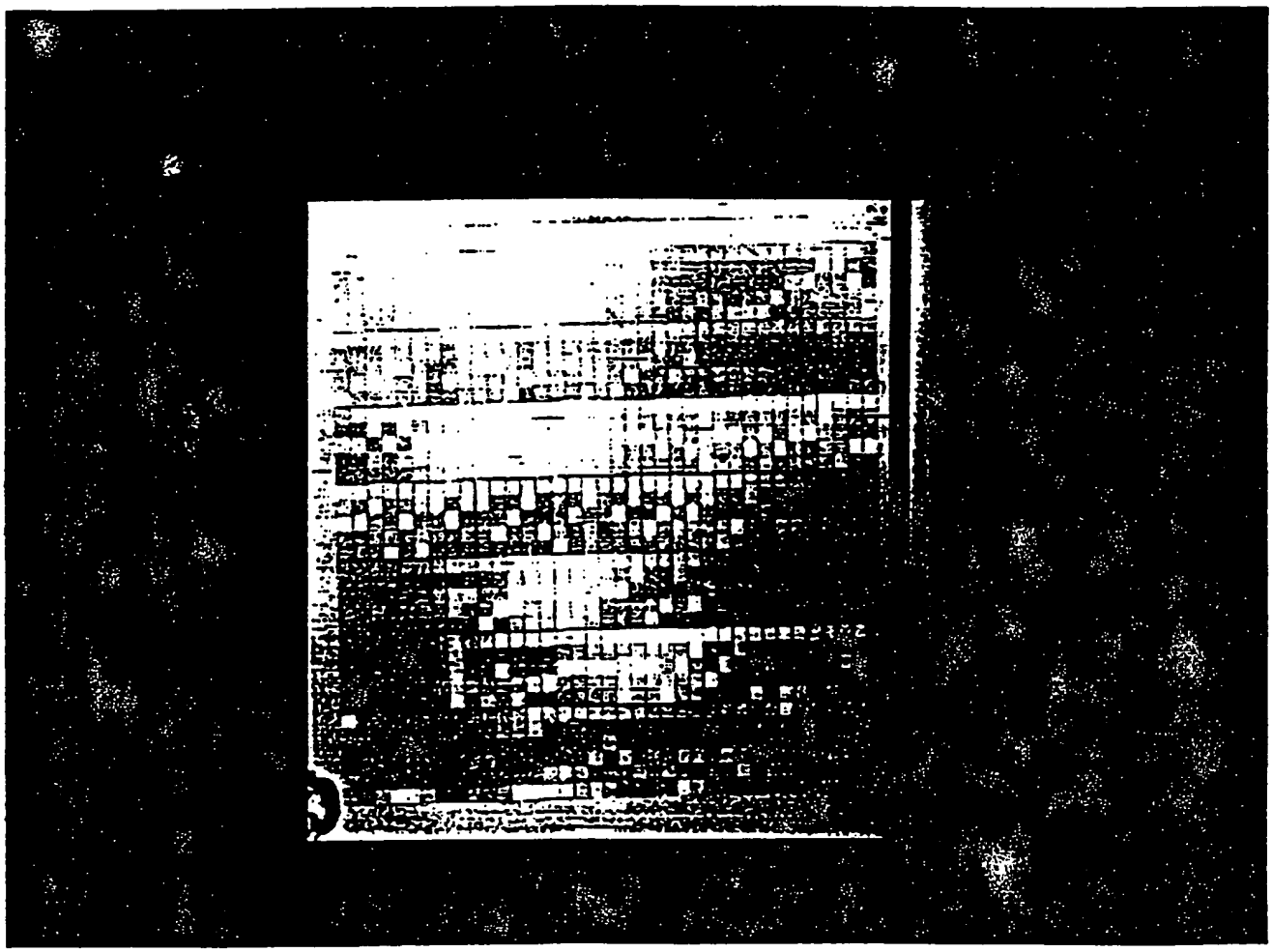


Fig. 33

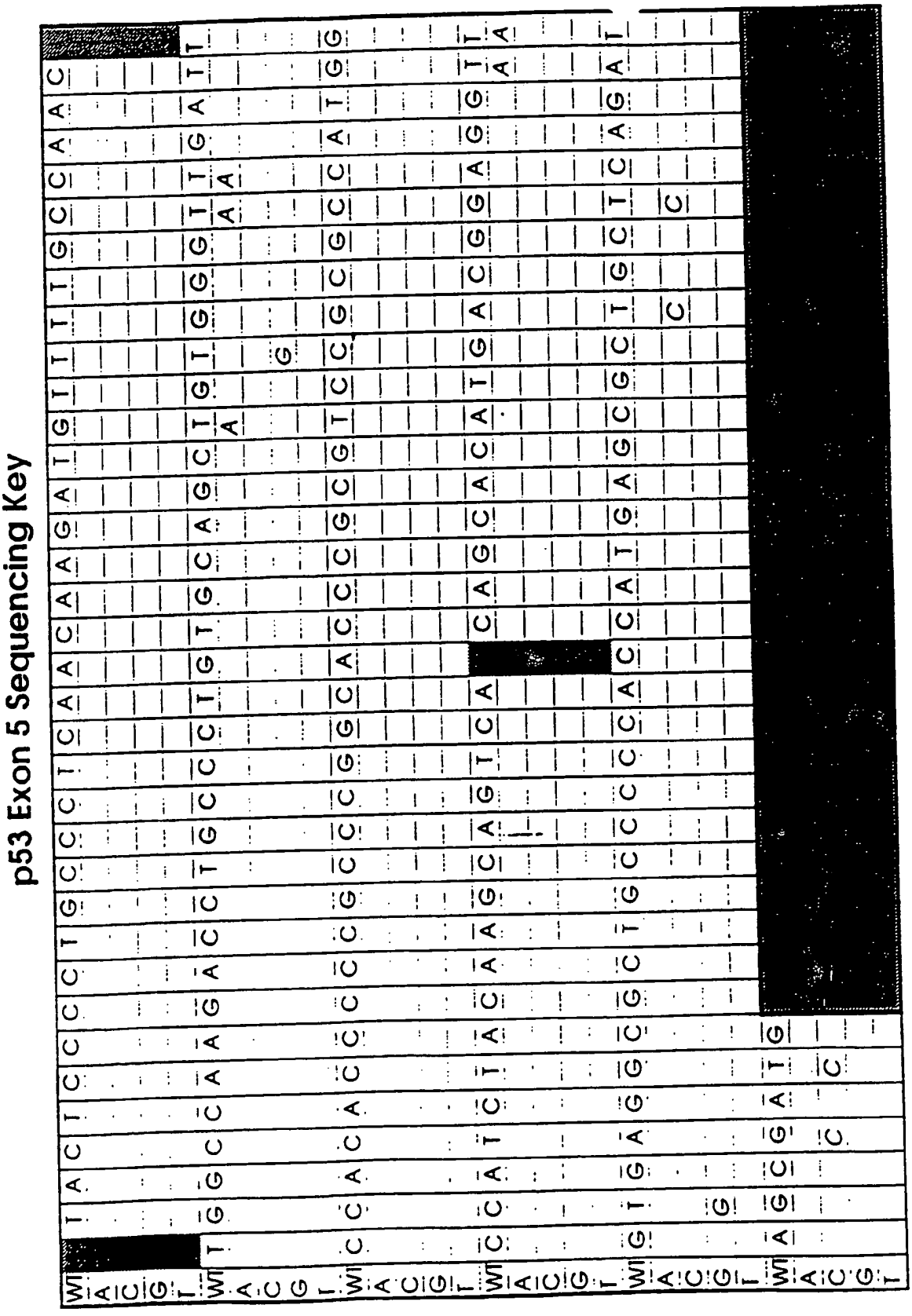


Fig. 34

THE HUMAN MITOCHONDRIAL GENOME

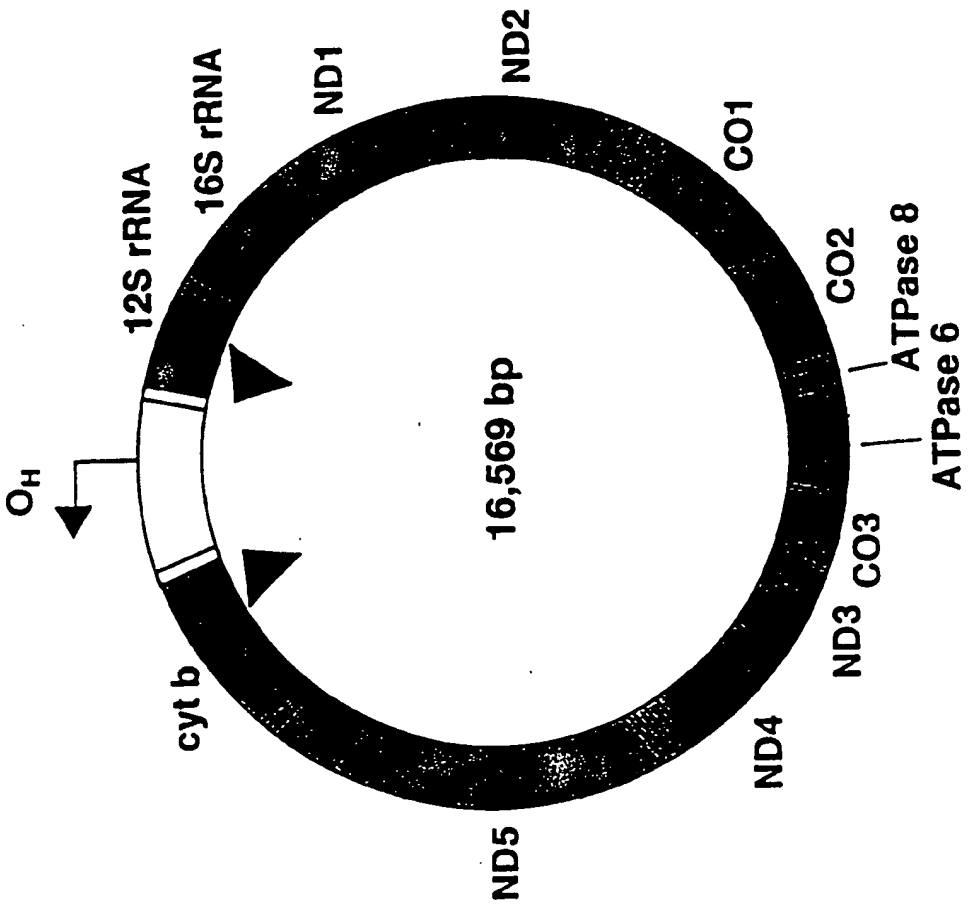


Fig. 35

HYBRIDIZATION

mt4

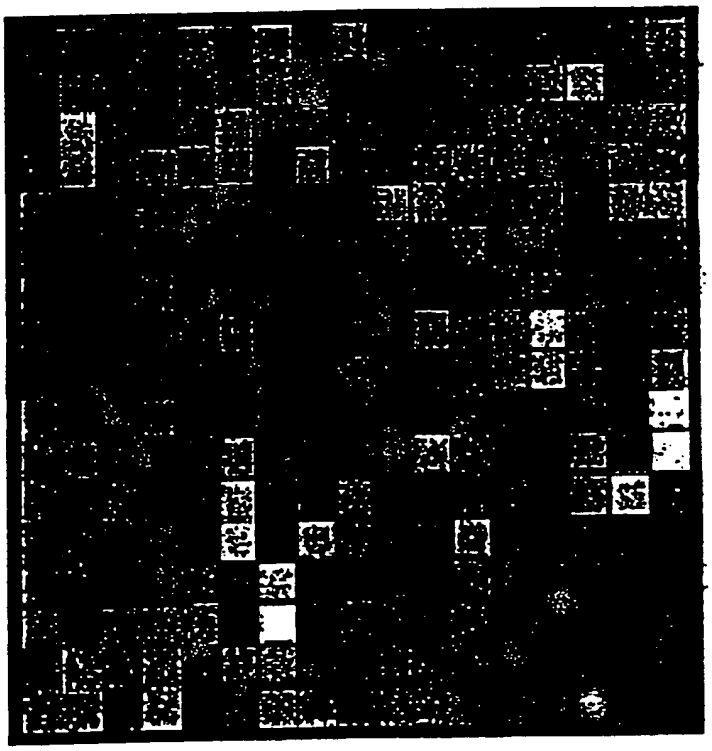
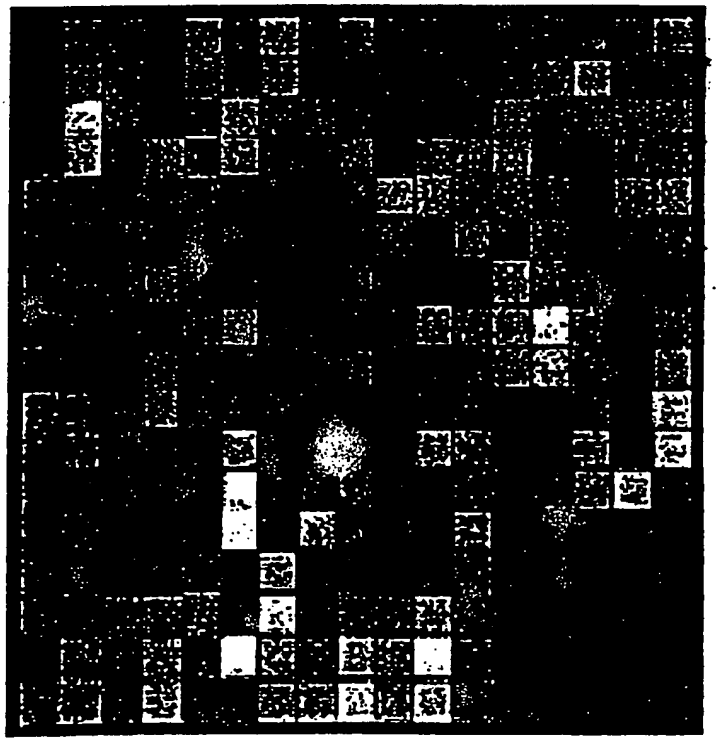


Fig. 36

mt5



HYBRIDIZATION

Fig. 37

PREDICTED DIFFERENCE IMAGE

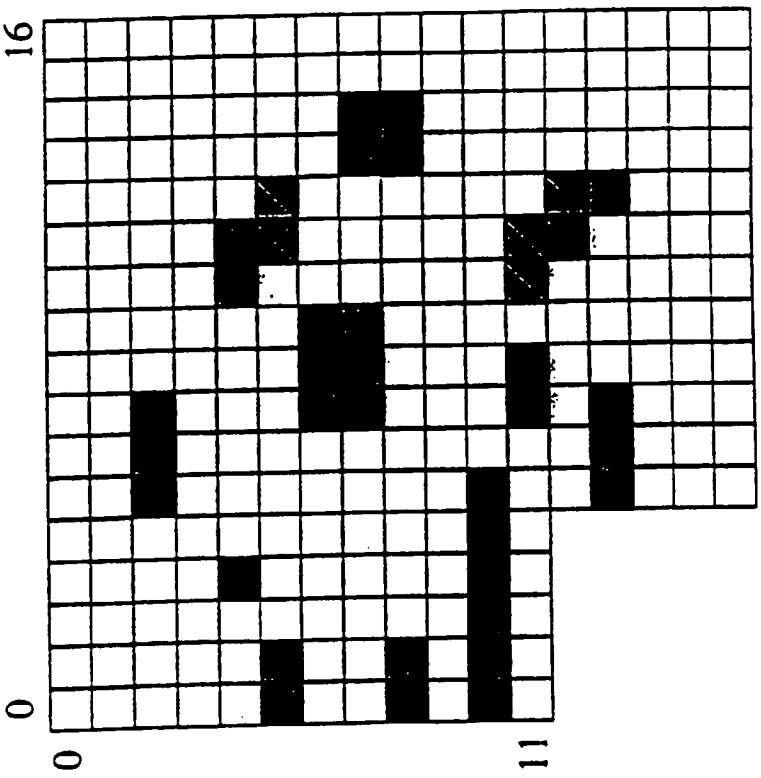


Fig. 38

DIFFERENCE IMAGE

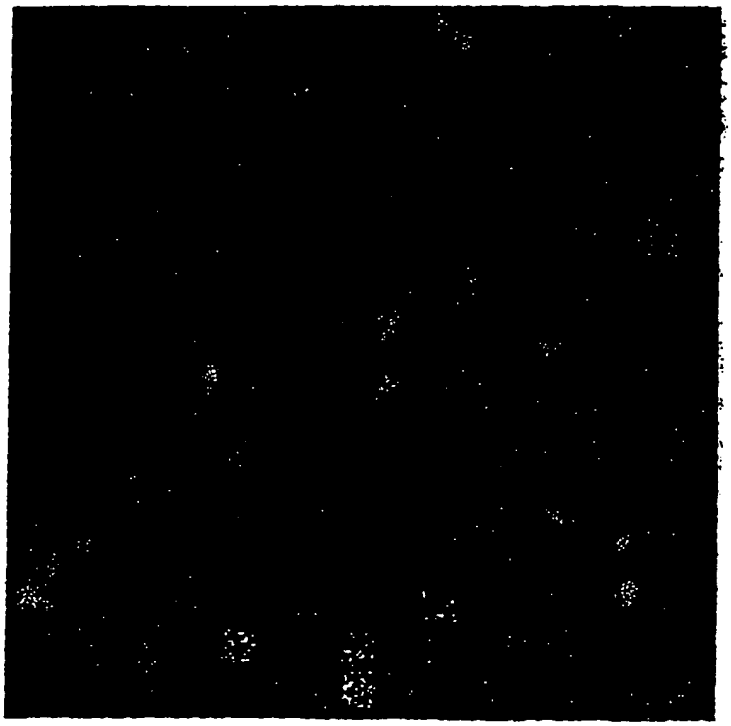
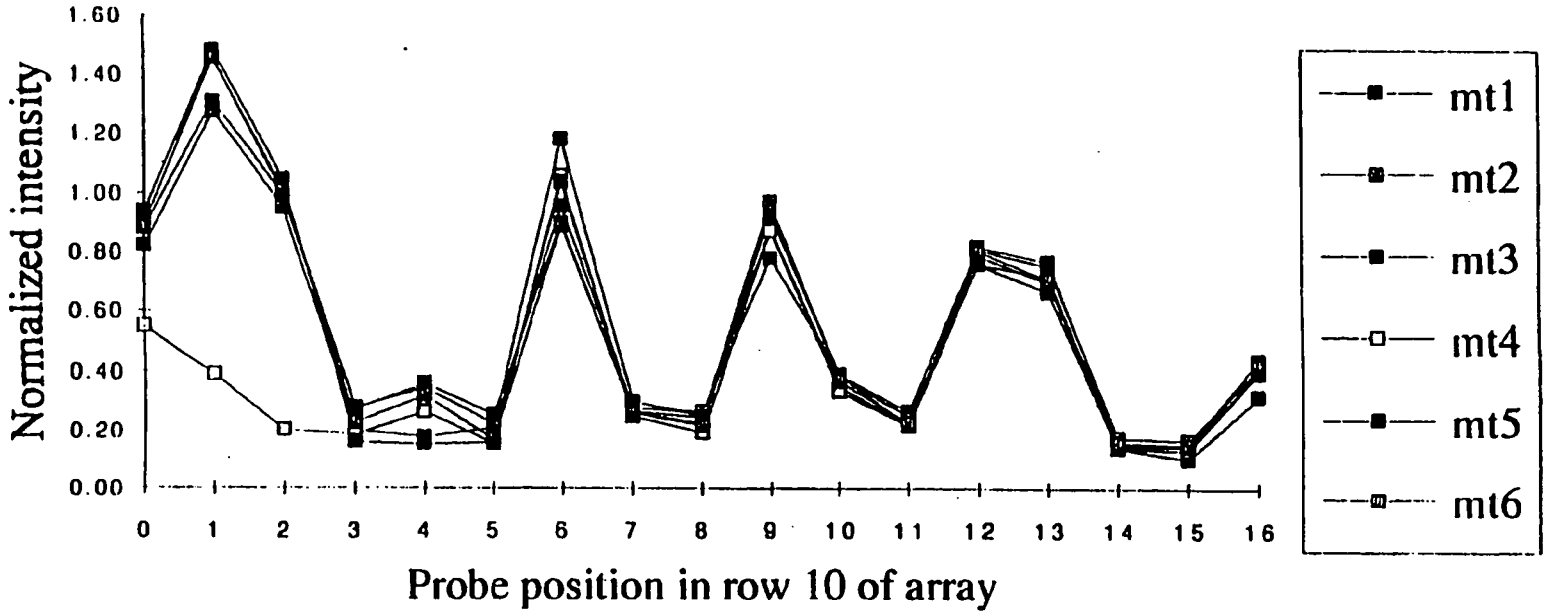


Fig. 39

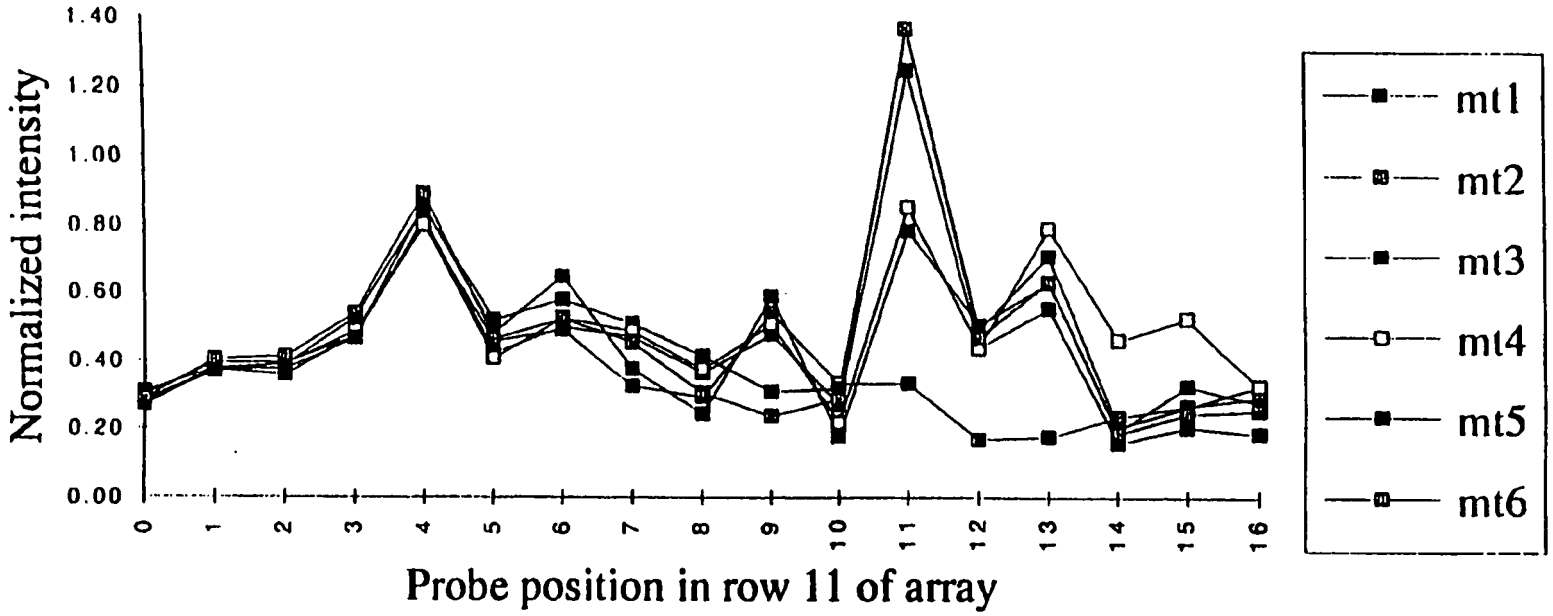
NORMALIZED INTENSITIES



probe position	0	1	2	3	4	5
probe length	13	13	12	12	12	12
sample (mt1 -> 6)	4	4	4	2, 5	2, 5	2, 5
mismatch position from 3' of probe	12	5	3	12	7	2
base change	t -> a	t -> a	t -> a	t -> c	t -> c	t -> c

Fig. 40
Sheet 1 of 2

NORMALIZED INTENSITIES



probe position	6	7	8	9	10	11	12	13
probe length	13	12	12	13	14	13	12	12
sample (mt1 -> 6)	2	2, 5	2, 5, 6	3, 6	3, 4, 5	2, 4, 5	2	2
mismatch position from 3' of probe	13	9, 10	3, 4 11	11, 5	4, 11, double	11, 3, double	6	3
base change	c -> t	c -> t	c -> t t -> c	t-> c	t -> c double	g -> a t -> c double	g -> a	g -> a

Fig. 40
Sheet 2 of 2

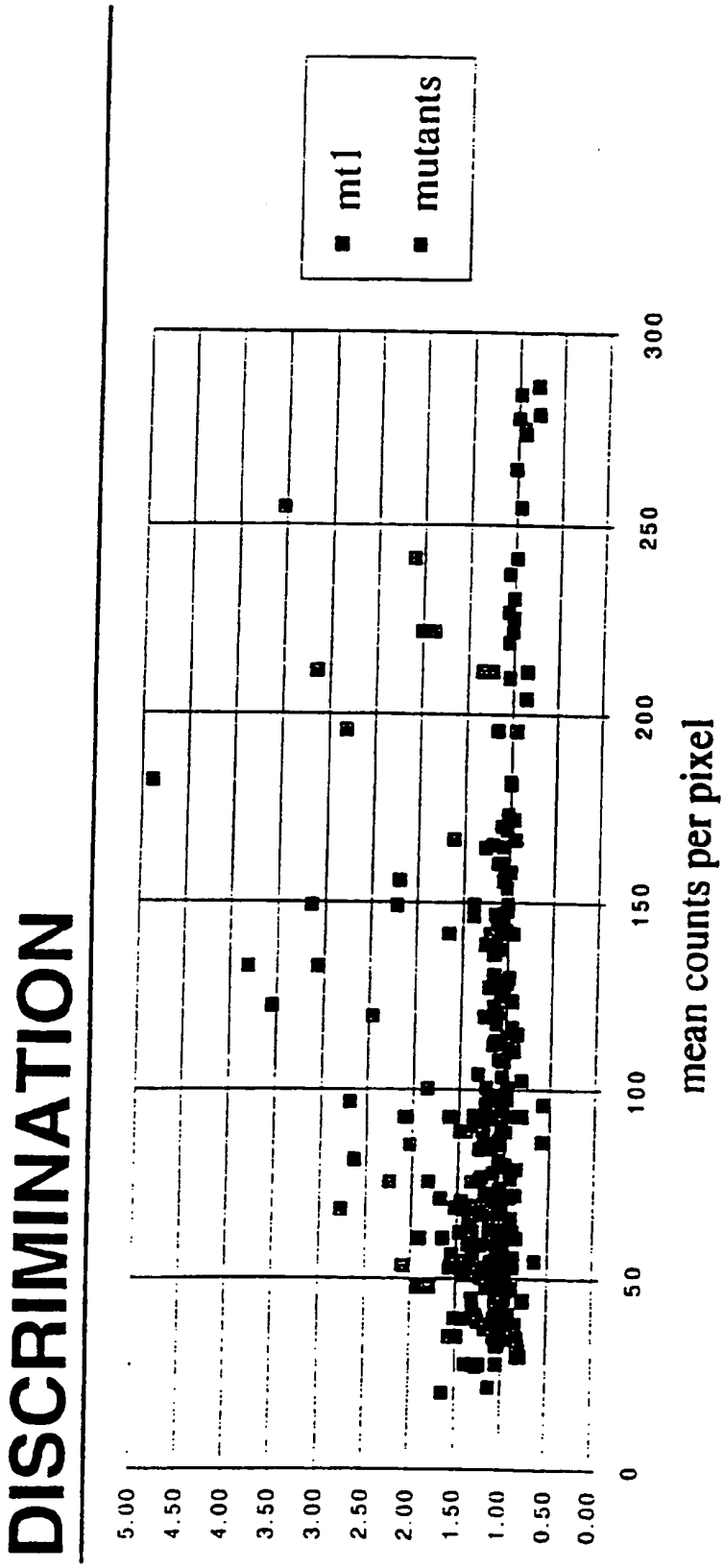

DISCRIMINATION
mt1
mutants
mean counts per pixel
0
50
100
150
200
250
300
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00

Fig. 41

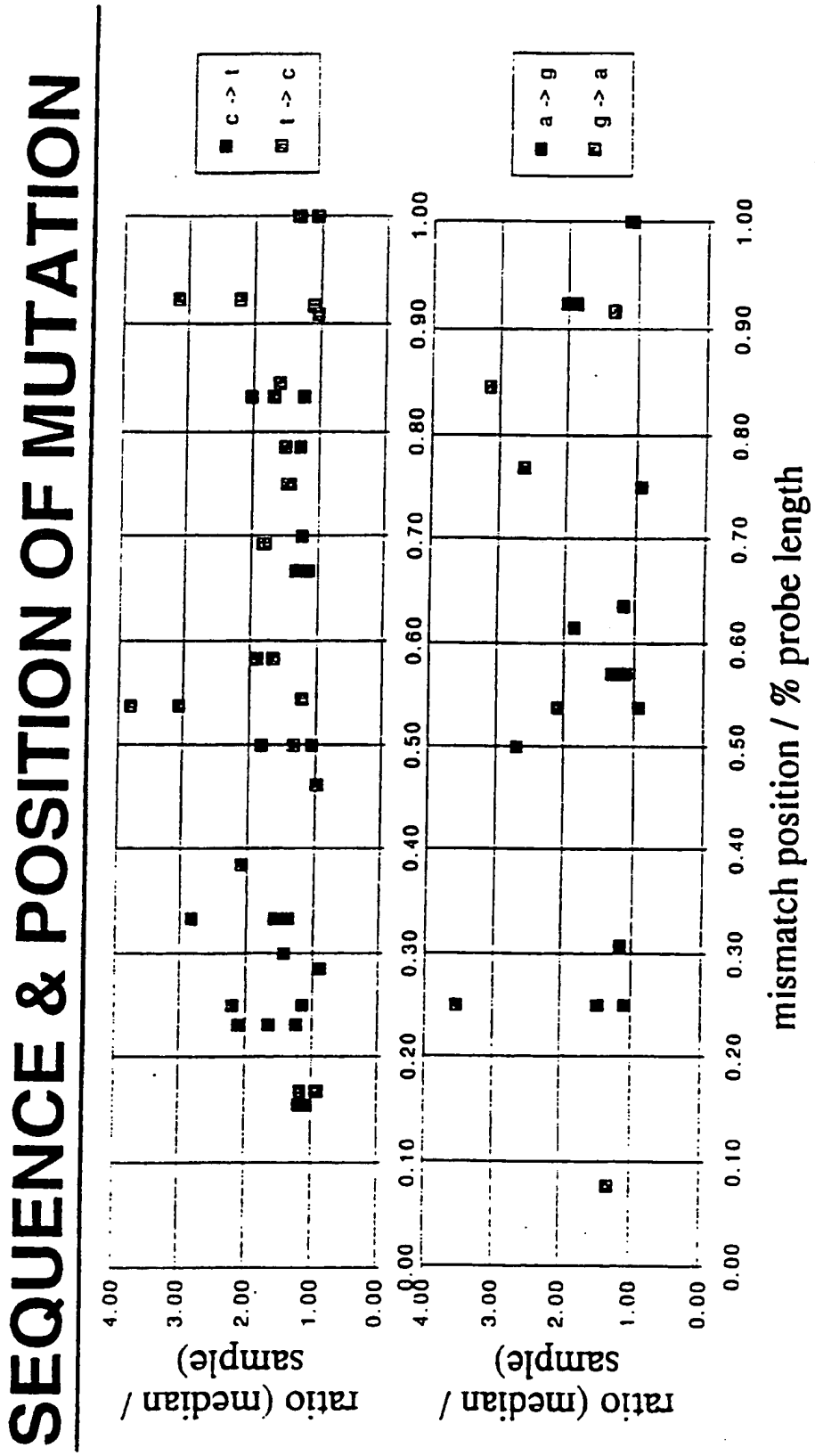

SEQUENCE & POSITION OF MUTATION
c -> t
t -> c
a -> g
g -> a
ratio (median / sample)
ratio (median / sample)
mismatch position / % probe length
0.00
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
0.90
1.00
0.00
1.00
2.00
3.00
4.00

Fig. 42

SEQUENCE

1 50

XaacaaacctacccaccccttaacagtacataagccatttacX

cgtacatagcacattacagtcaaaatccccttctcgtccccatggatgaccc

ccctcagataggggtcccttgaccaccatcccctccgtgaaatcaatatcccc

gcacaagagtgctactctcctcgctccgggcccataacacttgggggtag

ctaaagtgaactgtatccgacatctggttccctactttcagggTcataaagc

ctaaaatagcccacacgttccccttaaataagacatcacgatggatcacacag

gtctatcaccctattaaccactcacgggagctctccatgcatttggtatt

ttcgtctgggggtatgcacgcgatagcattgcgagacgctgggagccgga

gcaccctatgtcgcagtatctgtcttgattccctgcctcatcccTattatt

tatcgcacctacgttcaatattacaggcgaacatacttactaaaggtgt

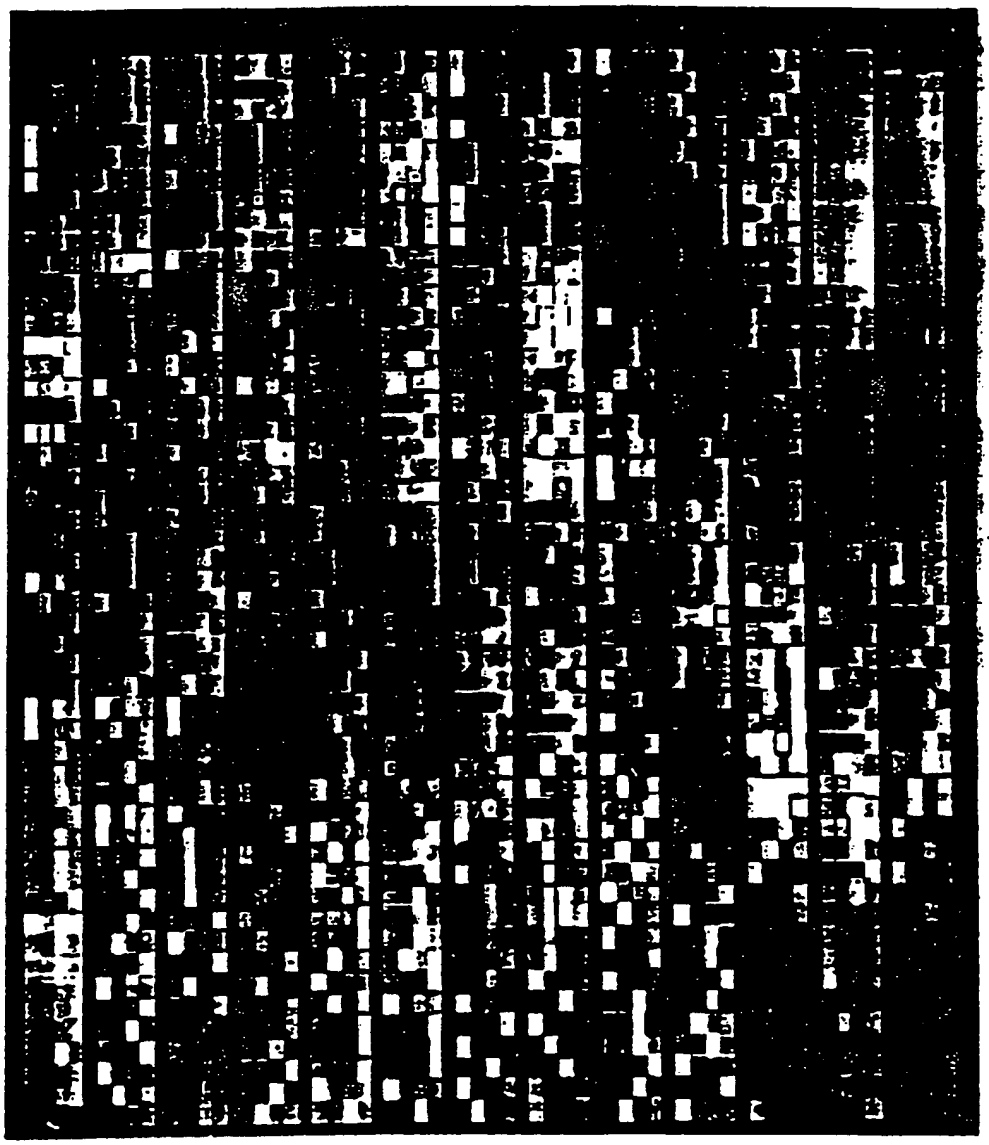
taatttaatttaatgcttgtaggacataataattaacaaattgaatgtctgcac

agccActtttccacacagacatcataacaaaaaattttccaccaaaccccccc

XctcccccgcttctgggccacagcacttaaacacatcTctgcccaaaccccX

Fig. 43

Fig. 44



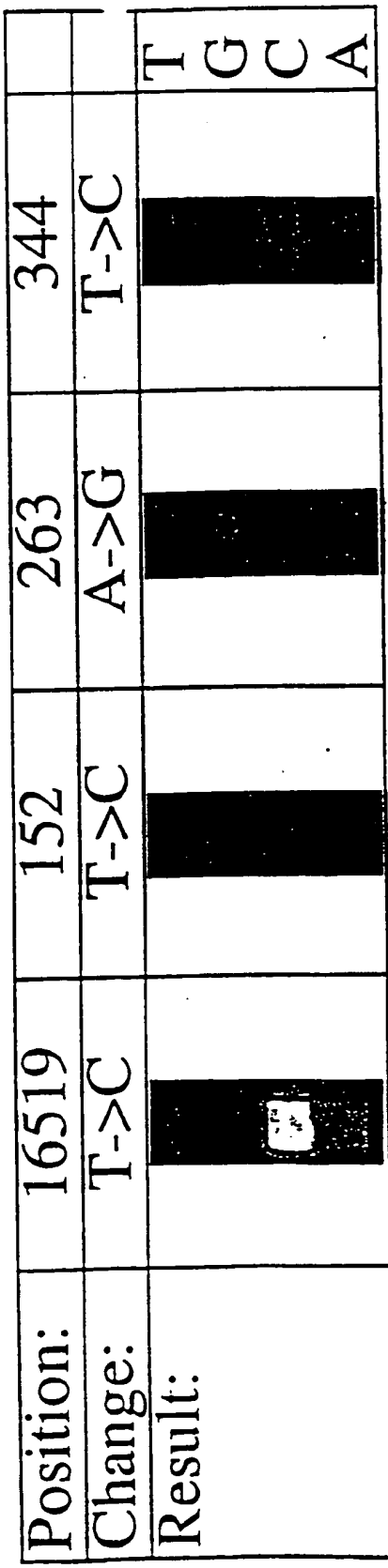


Fig. 45

Fig. 46

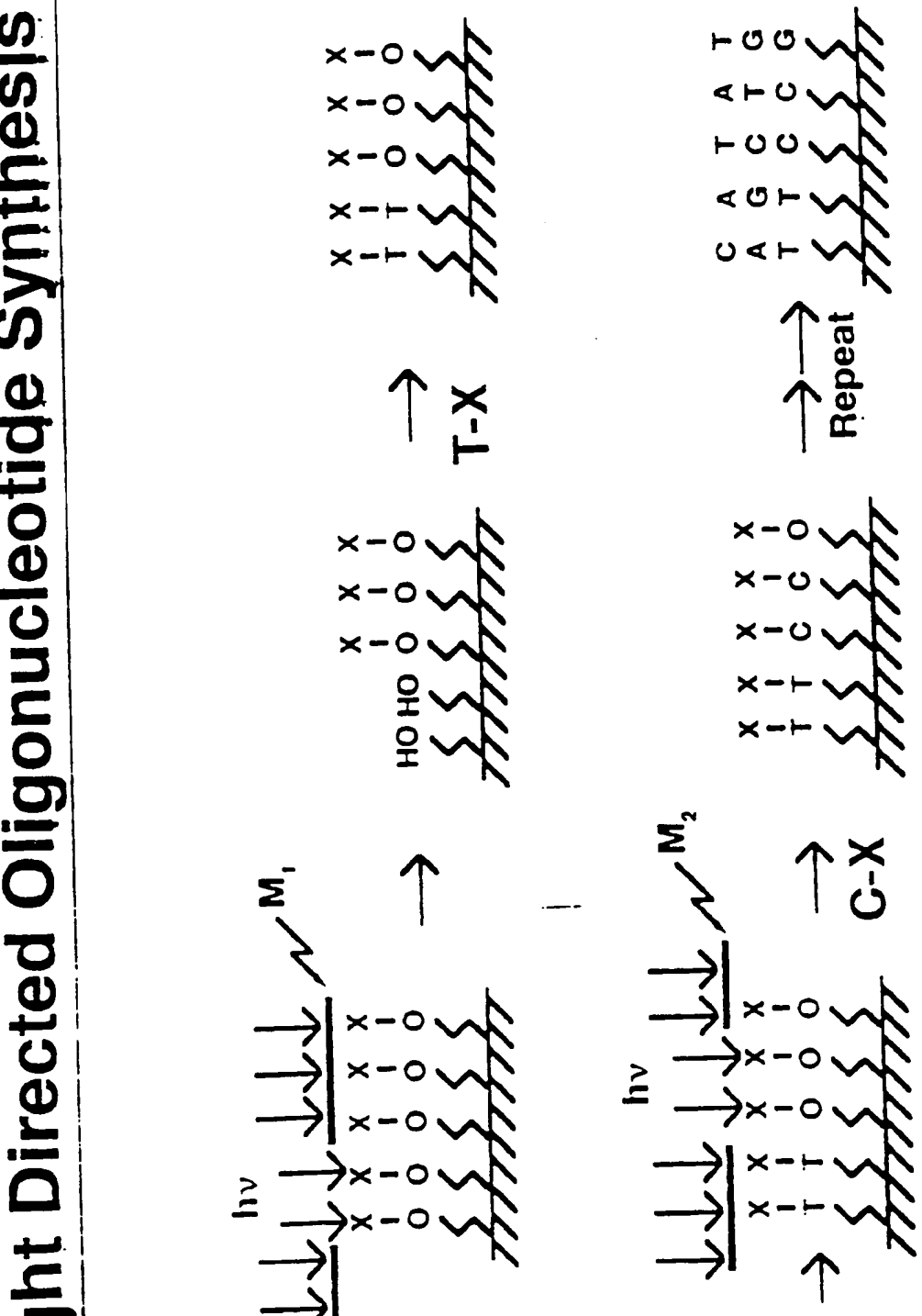

Light Directed Oligonucleotide Synthesis
hν
M1
T-X
HO HO
M2
C-X
Repeat

Fig. 47

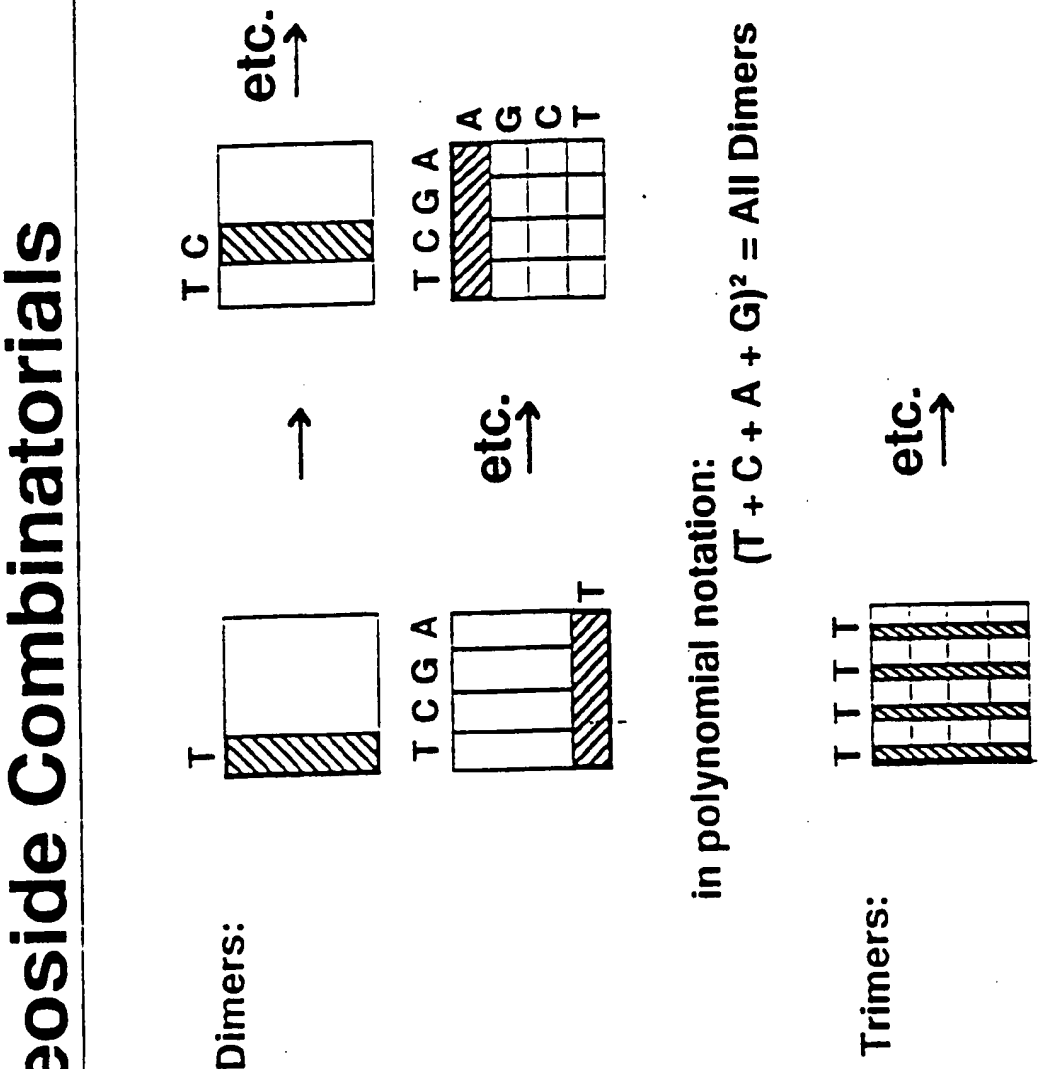
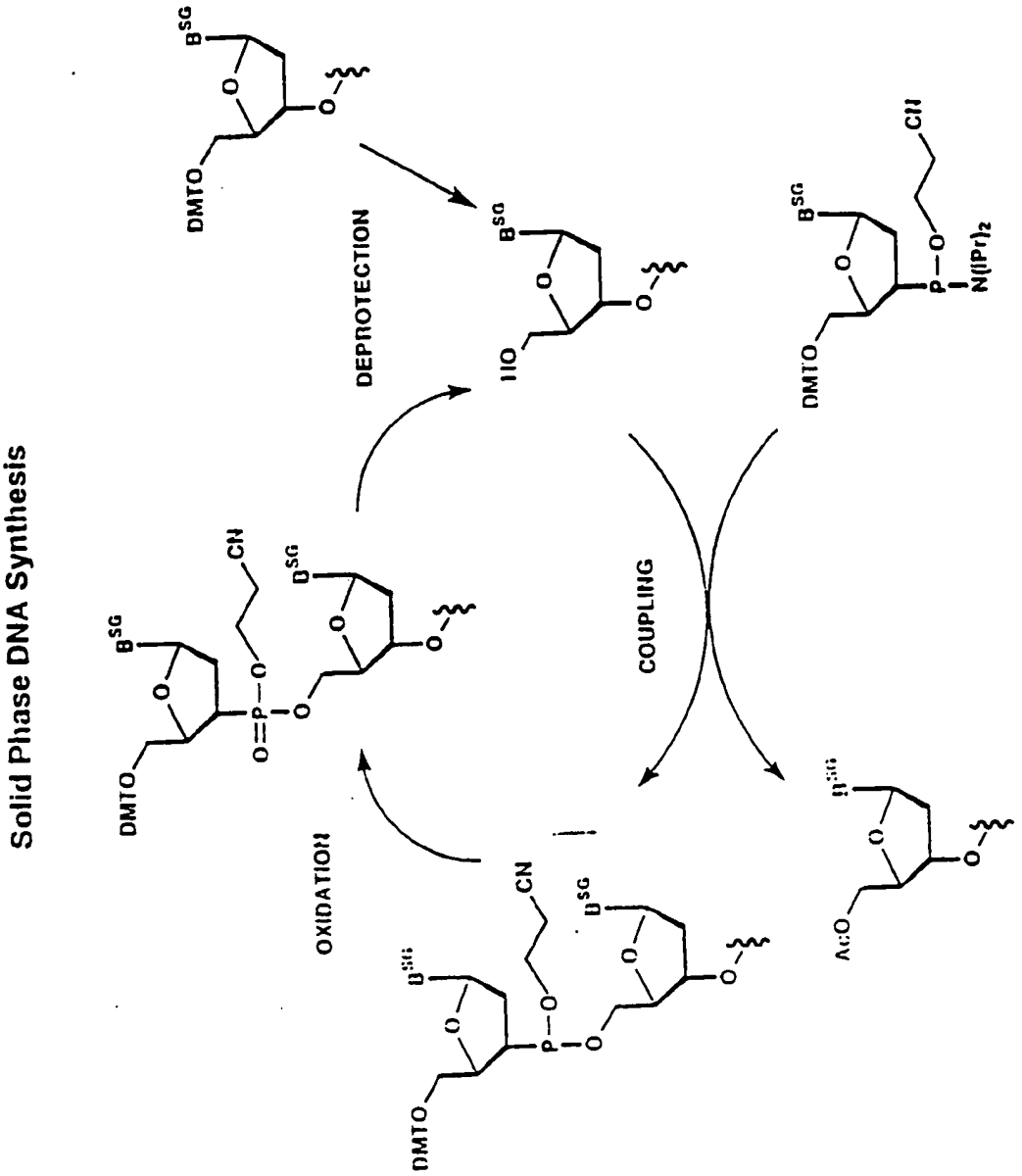

Nucleoside Combinatorials
Dimers:
T
T C
etc.
T C G A
T C G A
A G C T
etc.
in polynomial notation:
(T + C + A + G)² = All Dimers
Trimers:
T T T T
etc.

Fig. 48


Solid Phase DNA Synthesis
DEPROTECTION
COUPLING
OXIDATION
DMTO
HO
CN
N(iPr)2
Ac2O

Nucleoside Buildingblocks

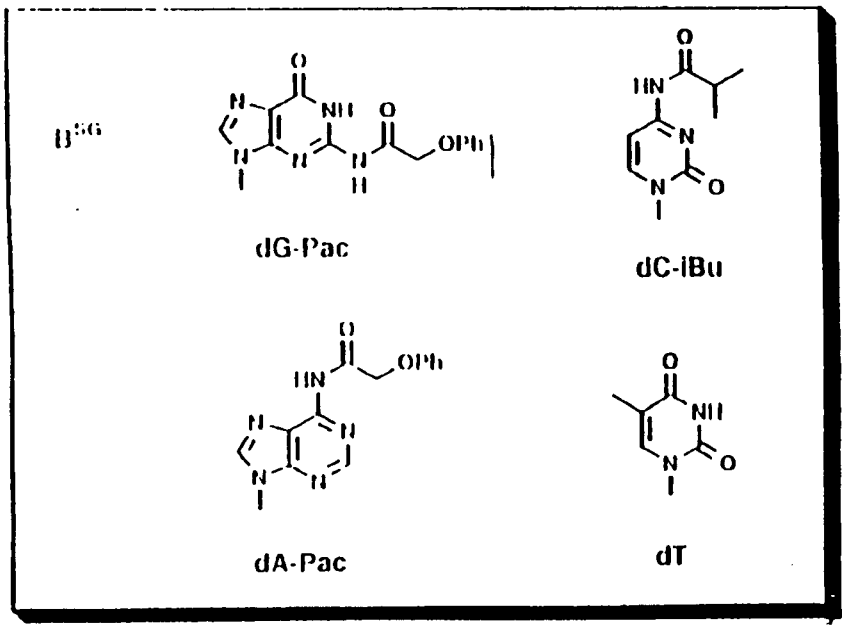


Fig. 49

Fig. 50

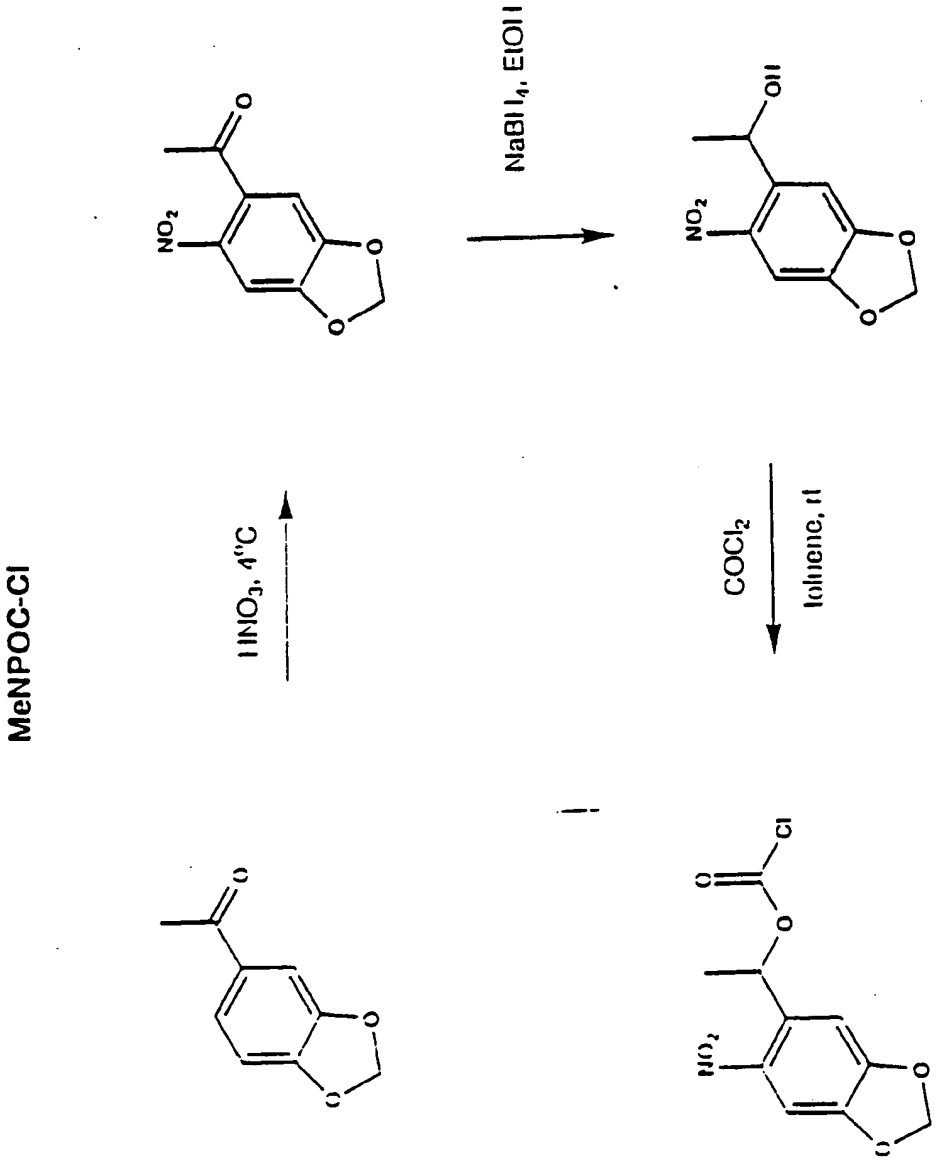
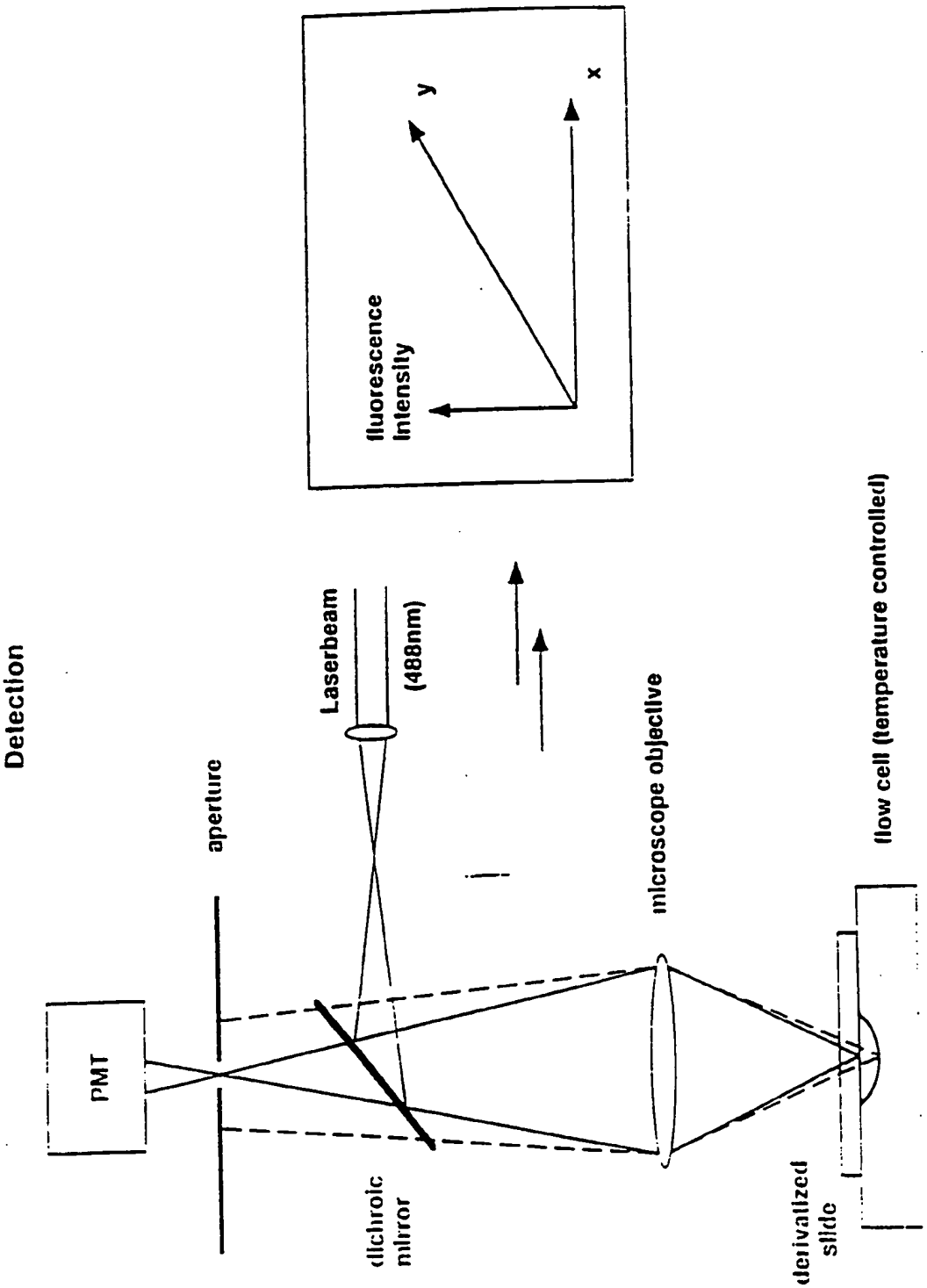


Fig. 51


fluorescence intensity
y
x
Detection
aperture
Laserbeam (488nm)
microscope objective
flow cell (temperature controlled)
PMT
dichroic mirror
derivatized slide